On the Structure and Neural Correlates of the Numerical Magnitude Representation and its Influence in the Assessment of Verbal Working Memory

Von der Philosophischen Fakultät der Rheinisch-Westfälischen Technischen Hochschule Aachen zur Erlangung des akademischen Grades eines Doktors der Philosophie genehmigte Dissertation

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Tag der mündlichen Prüfung: 30.06.2006

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Summary

This thesis is divided into two parts: The first part is concerned with the mental representation of numbers. It elaborates the structure of the mental representation of two-digit numbers and the process of integrating unit and decade magnitude information into a coherent two-digit number representation. The neural implementation of the comparison process of two-digit numbers is discussed. The second part investigates the impact of numbers in a working memory context: That is, do numerical semantics (numerical magnitude) influence performance in a task presumably assessing verbal working memory capacity.

The magnitude of two-digit numbers has been assumed to be represented along one analogue mental number line (Dehaene, Dupoux & Mehler, 1990). Dehaene and colleagues argued that if decades and units are represented separately, the effects of unit digits in a magnitude comparison task should be stronger when the unit digits appeared shortly before the decade digits. Indeed, they failed to find the hypothesized unit effects in a two-digit number comparison experiment with varied stimulus onset asynchrony (SOA) of units and decades. However, Nuerk and colleagues have obtained evidence for decomposed processing of decade and unit magnitude with a different set of stimuli (Nuerk, Weger, & Willmes, 2001). This set consisted of unit-decade compatible (i.e. both unit and decade digit comparison in a two-digit magnitude comparison task lead to the same result, e.g. 42_57, 4 < 5 and 2 < 7) and unit-decade incompatible (unit and decade digit comparison lead to divergent results, e.g. 47_62, 4 < 6 but 7 > 2) pairs of numbers. The reaction time (RT) advantage of unit decade compatible (henceforth compatible) number pairs as compared to incompatible lead Nuerk and colleagues (see Nuerk & Willmes, 2005 for a review) to the conclusion that a single access to one holistic magnitude representation is not sufficient for describing the mental representation of two-digit numbers. This RT difference is termed unit-decade compatibility (henceforth compatibility) effect.

The main objective of Study 1 was to examine whether the unit distance and compatibility effects obtained by Nuerk et al. (2001) get affected differently by SOA or not (cf. Dehaene et al., 1990). Such differences would be strong evidence that decades and units are indeed processed separately in two-digit number comparison. To examine unit-specific interference effects more comprehensively, three experiments were conducted: In Experiment 1 (i) the SOA range of Dehaene and colleagues was extended and (ii) a stimulus set was used where numerical distance of the unit digits was no longer restrained to the range of 1 to 4 like in the study of Dehaene and coworkers. Restraining the unit distance range to a maximum of 4 mitigates the influence of unit digit magnitude on the comparison process (Nuerk et al., 2001). In Experiment 2 number pairs from the same decade were included in order to further increase the salience of the unit digits since in Exp. 1 participants predominantly attended the decade digits which were informative in 100% of the trials. In Experiment 3 a procedural variation was employed to increase the salience of
the unit digits in a two-digit magnitude comparison task: The first pair of digits was always presented in the central axis of the screen. However, subjects could not know, whether this pair of digits represented the unit or the decade digits. This became clear only upon presentation of the second pairs of digits, either to the left or to the right of the first one. The main finding of Study 1 is that unit-related effects were strongly modulated by SOA. Moreover, attentional strategies influence the importance of the unit digit information for the task at hand. These results support the idea of decomposed processing of decades and units and thus indicate that two-digit numbers are not represented along a single holistic mental number line. Instead, at least additional representations for unit and decade digit information have to be assumed. It is discussed how the stimulus set and the experimental setting can alter number processing strategies even in a task as simple as two-digit magnitude comparison.

In Study 2 functional magnetic resonance imaging (fMRI) was used to investigate the neural correlates of two-digit number magnitude comparison process. Although simple at first glance, the comparison of two-digit numbers is a complex cognitive operation. It encompasses the encoding of object-based spatial relations of the constituting digits in both numbers, employing the place-value system and its rules to assign the correct numerical value to the digits, and a magnitude comparison process based on both decomposed and holistic magnitude information. By employing a parametric analysis approach, it was tried to disentangle these different aspects. Most importantly, the results of Study 2 imply that magnitude related and unit-decade compatibility related aspects recruit different, only partially overlapping structures within the parietal cortex along the horizontal aspect of the intraparietal sulcus (IPS). While the compatibility (or conflict) related components activate parts of the left medial bank of the IPS, a bilateral network of regions along the posterior IPS is activated by numerical magnitude. Within this latter network, no differential activation was observed that would imply a “numerotopic” organization of the IPS. That is, no evidence supports the assumption that the neural representation of magnitude information is spatially organized along the IPS according to the respective power of ten assigned to each digit.

In Study 3 a different approach was chosen to clarify the role of the hIPS in two-digit number magnitude processing. The question was whether the areas around the horizontal aspects of the intraparietal sulcus (hIPS) are functional necessary for solving this task and integrating unit-decade digit information of two-digit numbers. Transcranial magnetic stimulation (TMS) was used to modulate the excitability of the hIPS. If these regions are linked to the task at hand, a modulation of the cognitive effects under scrutiny indicates functional necessity. We employed low-frequency repetitive TMS (rTMS; 1Hz) which results in a virtual lesion. Virtual lesions are transient states of reduced excitability in circumscribed neural assemblies which last approximately half of the duration of stimulation. We stimulated over left hIPS and vertex as the control site. The most important finding is that for a subset of our sample we observed an increase of compatibility and
distance effects. These within-participant modulations of cognitive effects which served as markers for different underlying cognitive processes were limited in time. The specific modulation of the compatibility and distance effects were present for the first half of the experimental block but vanished in the second half. The results are discussed within a framework assuming (i) a different amount of transcallosal transfer for male and female participants and (ii) slightly different preferences of the left and right parietal cortex regarding the use of either decomposed or holistic magnitude information. Taken together, Study 3 corroborates the results from several imaging studies (among them Study 2) which found the hIPS to be involved in processing of numerical information. Moreover, the hIPS seems to be a good candidate area for mastering the integration processes that are required when two-digit numbers are processed.

In Study 4 it was investigated whether numbers are good candidates to serve as stimulus material in assessing verbal working memory (vWM). Although numbers carry averbal semantics (i.e. magnitude) they are often utilized in verbal working memory tasks. However, vWM is thought to rely on a purely phonological code. Here the influence of (i) averbal semantics and (ii) different tasks on performance in a vWM context was tested by examining stimulus and task specific variation of activity in the horizontal parts of the hIPS. The hIPS has previously been shown to subserve magnitude processing modulated by (i) specific stimuli and (ii) specific tasks. Two variants of an n-back paradigm (comparison and identity match tasks) utilizing letters and numbers as stimulus material at different levels of vWM load were administered. Behavioural and functional imaging data reveal stimulus specific modulation of activity in the hIPS suggesting a semantic influence of numbers. In the identity match task numbers induced additional hIPS activation compared to letters while letters never induced additional hIPS activation when compared to numbers. Letters as compared to numbers only induced additional hIPS activation in the comparison task. These results question the assumption of a purely phonological code in vWM because hIPS activation subserving magnitude processing is modulated by stimulus semantics and task demands.
1 General Introduction

This thesis is concerned with the mental representation of numbers. It tries to elaborate the structure of the mental representation of two-digit numbers and the process of integrating unit and decade related magnitude information into a coherent two-digit number representation. The neural implementation of the comparison process of two-digit numbers is discussed. Finally, a closer look is taken at the impact of numbers in a working memory context: That is, do numerical semantics (numerical magnitude) influence the performance in a task presumably measuring verbal working memory capacity.

To answer these questions several techniques from cognitive psychology and neuroscience were employed: Three classical reaction time (RT) experiments, two neuroimaging studies (functional magnetic resonance imaging, fMRI) as well as one experiment using transcranial magnetic stimulation (TMS) were conducted.

1.1 Theoretical Background

In the following, the properties and features of number processing will be elaborated on. A special focus will lie on the processing of two-digit numbers and its differences from the processing of single digits.

Numbers are a fundamental part of everyday-life. Virtually all activities involve the processing of numbers to at least some degree. However, the mapping between numerical magnitude ( numerosity) and the graphic and verbal symbols used to address numbers is arbitrary. That means, no feature of e.g. the visual form of Arabic numbers allows an understanding of their meaning at first glance, i.e. without some sort of formal education. For instance, the symbol “6” is visually more similar to “8” or “3” than to “5” or “7”. Nevertheless, the semantic meaning in terms of numerical magnitude of “6” is more similar to “5” and “7” than to “3” or “8”. Similar arguments hold for verbal number representations, i.e. number words.

However, formal education and the intense use of numbers allow very easy access to the numerical meaning of numbers. Even more intriguing is the finding that a number presented (visually or auditorily) activates the respective numerical meaning automatically and regardless of the task at hand. That is, even when the task does not require the numerical meaning of numbers but can be solved on the basis of knowledge about number parity (odd or even) information for example, the numerical magnitude influences manual responses of participants (e.g. Dehaene Bossini, & Giraux, 1993; Fias, Brysbaert, Geypens, & d’Ydevalle, 1996). In a parity judgment task, larger numbers are faster responded to with a right-hand key and smaller numbers are faster
responded to with a left-hand key (Dehaene et al., 1993). The effect is explained using the assumption of a left-to-right-oriented mental number line: If the location of the response is spatially congruent with the internal spatial representation of the number line (e.g. large numbers are on the right and response is on the right), RT is fast and otherwise slow. The influence of numerical magnitude information even prevails in situations that do not allow for conscious perception of the numbers. In a priming study, Naccache and Dehaene (2001) subliminally presented a masked number (prime) prior to the actual number stimulus (target) which had to be evaluated in a magnitude comparison task (i.e. is the present number smaller/larger than five?). The numerical distance between prime and target significantly influenced response latencies.

Although being symbolic and abstract, the numerical magnitude representation resembles other psychophysical dimensions. Two major effects from classic psychophysics have been observed using numbers instead of physical measures such as weight of loudness: The so-called distance effect and the size effect.

The distance effect describes the fact that in a magnitude comparison task response latencies are inversely proportional to the numerical distance between two numbers (Moyer & Landauer, 1967).

The size effect describes the fact that in a magnitude comparison task reaction time is positively correlated with the problem size, i.e. the larger the sum of a given pair of digits the larger the reaction time (e.g. Schwarz & Stein, 1998).

Especially the distance effect and the size effect provided the inspiration to describe the mental representation of number with the metaphor of a mental number line. That is, numbers are thought to be represented along a left-to-right-oriented, logarithmically compressed, continuous mental number line (e.g. Dehaene et al., 1993).
1.1.1 Magnitude Representation of Two-Digit Numbers

Differences between Number Magnitude Representations of Single- and Two-digit Arabic Numbers

Working with Arabic numbers larger than 9 requires mastery of the Arabic place-value system. For instance, when we have to represent a two-digit number from 10 to 99, we first have to encode different digits constituting this number. Furthermore, we have to correctly attribute the respective power of 10 to a particular digit depending on its spatial position in the two-digit string (e.g. in 23, the value of the 2 is $2 \times 10^1 = 20$ while in 32 the value of the 2 is $2 \times 10^0 = 2$). Therefore, the integration of two single digits into one two-digit number is a complex cognitive numerical process. Nuerk et al. (2001) have shown that semantic interference of unit and decade digit in two-digit number comparisons may lead to additional cognitive processing costs. In a magnitude comparison task with two-digit numbers, (compatible) number pairs are responded to faster when magnitude comparison of the corresponding unit and decade digits from both numbers lead to the same result (e.g. 42 vs. 57: 4 < 5 and 2 < 7) as compared to (incompatible) number pairs where these two comparisons lead to diverging results (e.g. 47 vs. 62, because 4 < 6 but 7 > 2; Nuerk, Weger, & Willmes, 2001, 2002, 2004; Nuerk & Willmes, 2005). This phenomenon is called the unit-decade-compatibility (henceforth compatibility) effect.

Evidence for separate processing of decade and unit magnitude

Nuerk and colleagues have questioned the conclusion that the magnitude of two-digit numbers is just processed holistically (Nuerk, Weger & Willmes, 2001, 2002, 2004, 2005). They investigated two-digit number magnitude representation by manipulating unit-decade compatibility. As introduced above, in a two-digit number comparison task (e.g., 42 vs. 57, short. 42 vs. 57) a given number comparison is defined as unit-decade compatible if both comparisons between decades and units lead to the same decision (e.g., for 42 vs. 57, both 4 < 5 and 2 < 7). A number comparison is defined as unit-decade incompatible, if the two comparisons for units and decades lead to different decisions (e.g., for 47 vs. 62; 4 < 6, but 7 > 2). Note that absolute overall distance is 15 in both cases. If a single analogue mental number line was sufficient to represent magnitude, then no compatibility effect should be obtained. However, incompatible number pairs were responded to more slowly than compatible number pairs (Nuerk et al., 2001).

Is the compatibility effect perceptual in nature?

In their original study, Nuerk and colleagues (2001) have presented the two two-digit numbers in a vertical arrangement, i.e. above each other. Therefore, one might argue that the participants have engaged in a column-wise comparison of the respective digits. If so, the effect may be perceptually driven. This would limit the conclusions that can be drawn. However, Nuerk and colleagues have conducted a second experiment (Nuerk, Weger et al., 2004) using the same stimulus set. This time the stimuli were presented diagonally above each other. This stimulus
arrangement discouraged any strategy of comparing the digits in a column-wise fashion. Nevertheless, the compatibility effect was present with this stimulus arrangement, too. Thus, the compatibility effect for Arabic notation is not due to the particular choice of the perceptual setting.

**Semantic or response conflict**

A second objection against the compatibility effect is that it might reflect a pure response competition rather than central semantic interference between unit and decade magnitude. However, an important interaction between compatibility and unit distance can be observed (e.g., Nuerk et al., 2001) indicating that the compatibility effect is not only due to a magnitude-independent response conflict but that the magnitudes (and the distance) of the two different unit digits are processed. The compatibility effect was larger in trials with a large unit distance (e.g. 38_51) as compared to trials with a small unit distance (e.g. 43_52), although overall distance was held constant between the respective stimulus groups.¹ If the compatibility effect was located at the response level only, such an interaction with purely semantic stimulus properties would be hard to reconcile. Moreover, in a recent medical doctoral thesis, Clemens (in preparation) conducted a magnitude comparison task with a similar set of stimuli and simultaneously registered the electroencephalogram from 61 electrodes. If the compatibility effect was due to a mere conflict of response alternatives, one would expect a positive deflection of the so-called lateralized readiness potential (LRP) in incompatible trials. The LRP indicates the preparation of motor responses in advance of the actual execution. A positive deflection of this component in incompatible trials would indicate that the “wrong” response had initially been prepared, while the correct response was executed instead. Most importantly, no such negative deflection was observed, clearly speaking against the interpretation of the compatibility effect reflecting a mere response conflict.

**Language effects**

Initially, the compatibility effect was observed in a sample of native German participants. In German, the sequence of unit and decade information in number words and spoken numbers is inverted. For instance, an Arabic number like “21” is spoken as “ein-und-zwanzig”, literally “one-and-twenty”. This inversion property of German number words and spoken Arabic numerals might be responsible for the compatibility effect, since the incompatible unit information is processed before the relevant decade information due to a left-to-right reading bias in Western cultures. If this was true, the compatibility effect should be absent in participants whose mother tongue does not have the inversion property of number-words (strong language specificity hypothesis). Such a language is English. Therefore, Nuerk and colleagues (Nuerk, Weger et al., 2005) conducted a compatibility experiment with native English speakers. In contrast to the prediction of the strong

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¹ Note that distance was held constant between stimulus groups. For absolute unit distances other than 5 it is not possible to hold overall distance constant between individual compatible and incompatible trials with the same absolute unit distance.
language specificity hypothesis, the compatibility effect was replicated for Arabic number notation. It was diminished in effect size, however. Therefore, the authors argue in favour of a weak language specificity account: The compatibility effect is modulated by language but not fully determined.

**Notation-specific effect**

One might argue that the compatibility effect is notation specific, i.e. restricted to the Arabic notation. However, the original study of Nuerk and colleagues (2001) comprised a verbal condition: In addition to the Arabic number pairs, the same stimuli were presented as number words. As for Arabic notation, incompatible number pairs were responded to more slowly than compatible pairs in the verbal notation. This can be interpreted as first evidence for the view that the compatibility effect is not notation-specific.

One might argue that the same interaction of compatibility with unit distance for instance needs to be observed to make the effect notation-unspecific. Indeed, in the verbal notation compatibility did interact with unit distance in the predicted direction: Large unit distance incompatibility tended to lead to larger deteriorating effects in German number words (Nuerk et al., 2002). For small unit distances, a reversed effect emerged: Compatible magnitude comparisons were slower than incompatible ones. The reason for this finding may be simple, but very relevant for the SOA manipulation in Study 1 (see below). Overall distance was matched between groups of compatible and incompatible items. To compute the overall distance in compatible trials, the absolute unit distance has to be added to the decade distance in compatible trials. For instance, for 42_57 the decade distance is 1 (5 – 4 = 1 for the decade digits) and the absolute unit distance is 5 (7 -2 = 5). The overall distance is composed of 1 x decade distance plus 5 x unit distance. To compute the overall distance in incompatible trials, the absolute unit distance has to be subtracted from the decade distance in compatible trials. For instance, for 47_62 the decade distance is 2 (6 – 4 = 2 for the decade digits) while the absolute unit distance is again 5 (7 -2 = 5). Now the overall distance is composed of 2 x decade distance minus 5 x unit distance. This composition must necessarily lead to a larger decade distance in incompatible trials when overall distance is matched (see Figure 1). For English number words, a marginally significant inverted effect was found as well (Nuerk, Weger et al., 2005). When number words start with the relevant decade number word (e.g. “twenty-one”), participants seem to be able to focus only or predominantly on the decade number words. Consequently, they seem to exhibit an inverted compatibility effect. In both cases, the inverted compatibility effect is an expression of the ordinary numerical distance effect for the relevant decade digits rather than being related to compatibility.
Figure 1: Exemplary stimulus pairs. Unit distance must be added in compatible and subtracted in incompatible trials. In order to match both pairs in terms of overall distance (here: 15), the decade distance must be larger in incompatible number pairs.

Unit-Decade Integration

The compatibility effect is not only indicative of magnitude processing per se. It also marks the process of integrating the relative numerical value of digits constituting two-digit numbers in accordance with their position. If decade and unit digits are not parsed correctly into the place-value system, incompatible trials should produce more errors and slower RT than compatible trials because the irrelevant unit digit comparison may be inhibited insufficiently and may be in some cases mistaken for the relevant digit decade comparison. Then participants will produce an error in the incompatible condition, because in this case the unit comparison leads to a different response than the overall comparison. In the compatible condition, however, they do not produce an error, because the unit comparison is consonant with the correct response.

Evidence for a Holistic Analogue Magnitude Representation

The above compatibility effect evidencing separate processing of decades and units for two-digit numbers is not inconsistent with the results of the first three experiments of Dehaene et al. (1990). Dehaene and colleagues (1990) investigated two-digit number magnitude comparison and replicated the distance effect (cf. Moyer & Landauer, 1967): RT was reduced logarithmically with increasing distance from the standard, e.g. when compared to 65, the number 51 yielded faster responses than the number 59. In particular, Dehaene and colleagues found no convincing evidence for a separate representation of decade and unit magnitude, concluding that the magnitude of two-digit numbers is represented holistically (see also Brysbaert, 1995; Reynvoet & Brysbaert, 1999). Indeed, Dehaene and colleagues were well aware that besides a holistic model based on an analogue mental number line the so called interference model based on separate comparisons for decades and units captures “the essential features of [their] comparison data” (Dehaene et al., 1990, p. 634) for a stimulus onset asynchrony (SOA) of zero in their first three experiments (cf. also Hinrichs, Yurko, & Hu, 1981, for early suggestions of the interference model).
To distinguish between these alternative accounts, Dehaene et al. (1990) used the SOA manipulation method which has been successfully applied to investigate interference effects in other domains (e.g. Glaser & Glaser, 1982; for the Stroop effect). Dehaene and colleagues conducted a fourth experiment in which they manipulated the SOA (-50ms, 0ms, +50ms) between presentation of the decade and unit digit. The authors argued that the units would create more interference if they are presented before the decade digits because then more activation accumulated for the irrelevant unit magnitude processing than when they are only presented after the decade digits. The major argument for rejecting the interference model was the observation that the regression slopes of the influence of units did not significantly differ between the three SOA conditions, i.e. between the decade-first and the unit-first conditions.

**Stimulus Choice as a Possible Reason for the Null Effect Indicating Analogue Magnitude Representation**

A possible reason why Dehaene and colleagues did not find significant slope alterations may have been the (fixed) standard number 55 which they have used in their SOA experiment. This restricts unit distance between standard and target to a maximum of 4. As described above, the compatibility effect interacted with unit distance. For German number words, a regular compatibility effect for larger unit distances was observed, while even a negative compatibility effect emerged for smaller unit distances (Nuerk, Weger et al., 2002). For children in third and fourth grade, the same interaction was observed (Nuerk, Kaufmann, Zoppoth, Willmes, 2004). For larger unit distances a regular compatibility effect tended to be observed, while for smaller unit distances a negative or a null effect was found. In sum, restricting the unit distance to a range from one to four as in Dehaene’s experiments increases the probability of finding a null effect. A closer examination of Dehaene’s data seems to be numerically consistent with such a hypothesis. Dehaene et al. have found numerically somewhat smaller unit slopes for the decade-first condition, possibly indicating a weaker role of the magnitude of units when the decade is presented first. If this finding reached significance, it would be consistent with the notion that decades and units are processed separately. It is thus well possible that larger unit distances would lead to a larger and significant unit distance effect.

This hypothesis can be tested with the stimuli set of Nuerk et al. (2001) because compatibility effects for large and for small unit-distance stimuli can be compared. If a significant SOA alteration of the compatibility effect is obtained for large unit distances, this would be inconsistent with the interpretation of Dehaene and colleagues. Furthermore, if no significant or at least a smaller modulation would be obtained for small unit distances, this would be consistent with an alternative explanation of Dehaene’s data stating that the null effects for the unit regression slopes may be due to the specific stimulus set used with a fixed standard of 55 resulting in only small unit-distance trials.
Moreover, the existence of an inverse compatibility effect (see above) offers interesting perspectives: When the decade digit is presented first and is then processed predominantly, we should rather observe inverse compatibility effects. In contrast, when the unit digit is presented earlier, we may observe interference between units and decades, namely regular compatibility effects as observed in Nuerk et al. (2001).
1.1.2 The Neural Correlates of Number Magnitude Processing

Number processing is known to rely on parietal structures. Converging evidence comes from studies using different approaches such as fMRI (e.g. Pinel, Piazza, Le Bihan, & Dehaene, 2004; Fias, Lammertyn, Reynvoet, Dupont, & Orban, 2003; Piazza, Izard, Pinel, Le Bihan, & Dehaene 2004), positron emission tomography (PET; e.g. Thioux, Pesenti, Costes, De-Volder, & Seron, 2005), TMS (e.g. Goebel, Walsh, & Rushworth, 2001), or patient records (e.g. Delazer, Benke, Trieb, Schocke, & Ischebeck, in press). A common finding is that activity in large proportions of the parietal cortex is inversely proportional to the numerical distance of two numbers in a magnitude comparison task. Using the phenomenon of repetition suppression (i.e. when a stimulus is presented two times the activity in a given brain area is reduced upon the second presentation), Naccache and coworkers (2001) have shown that activity in parietal cortex is not due to a confound of difficulty and numerical distance. Processing numerical distance is by far not the only numerical function that relies at least partially on the parietal cortex. The parietal cortex has recently been subdivided in several ways to allow for a more fine-grained mapping of different numerical functions (Cohen Kadosh et al., 2005; Dehaene, Piazza, Pinel, & Cohen, 2003). In their review, Dehaene and colleagues (2003) have postulated the differential involvement of three parietal structures: First, left angular gyrus (AG) is supposed to support representation and manipulation of verbal numbers. Second, bilateral posterior superior parietal cortex (PSPL) is active when (spatial) attention has to be shifted along the mental representation of numbers (i.e. the mental number line). Finally, areas around the horizontal part of the intraparietal sulcus (hIPS) are activated bilaterally whenever numbers are perceived or processed, irrespective of notation or conscious processing (e.g., Naccache and Dehaene, 2001; Delazer et al., 2003). The bilateral region of the hIPS is the main candidate area for a neural correlate of numerical magnitude representation. Hubbard and colleagues (among them Dehaene; Hubbard, Piazza, Pinel, & Dehaene, 2005) have recently changed this terminology slightly: In their review they have developed a fine-grained differentiation of the specific parietal structures and their involvement in number processing. Regions located in the ventral intraparietal region (vIP) are postulated to be crucially involved in representing numerical magnitude. The human homologue of the macaque area lIP (lateral intraparietal sulcus), on the other hand, is hypothesized to be involved in “programming overt and covert shifts to the contralateral side of space” (Hubbard et al., 2005; p. 445; Note that according to Culham and Valyear (2006), the human homologue of lIP is situated on the medial bank of the IPS, rather than on its lateral aspects). A third region around the intraparietal sulcus, located in the anterior aspect of the IPS (aIPS) is associated with grasping objects and action observation. Note that in the work of Hubbard and colleagues the area aIPS covers large aspects of both areas around the postcentral sulcus and anterior aspects of the hIPS.
Most importantly, they postulate that bilateral ventral intraparietal regions (vIP) are most fundamental for representing numerical magnitude.

1.1.2.1 Transcranial Magnetic Stimulation Studies Examining Number Representations

Most of the above conclusions about the neural basis of number representations have been inferred from studies employing imaging techniques such as fMRI or PET. However, with these techniques brain activation is only observed as a dependent variable while the participant performs a given task. The mere (co)activation of a given brain area does not prove its functional necessity for the task at hand. Transcranial magnetic stimulation can be regarded as a complementary technique since it temporarily modulates activity of specific brain areas in (healthy) participants. Thus, brain activity is no longer an observed dependent variable; rather it can be manipulated as an independent variable. Therefore, TMS can be used to probe postulated links of certain brain areas with specific cognitive functions (Robertson, Theoret, & Pascual-Leone, 2003; Lavidor & Walsh, 2004). Nonetheless, only a few TMS studies have been published so far examining the neural basis of number processing.

Goebel et al. (2001) applied repetitive TMS (rTMS) over left and right AG and supramarginal gyrus (SMG) as a control site while participants performed a two-digit number comparison task with a fixed standard. The authors found RT to be modulated by an interaction of stimulation site, distance from the standard and numerical size. In detail, when TMS was applied over the left AG, participants responded more slowly in trials with numbers larger than 65. This interaction was modulated by numerical distance from the standard, i.e. RT increased with decreasing distance of numbers larger than 65 from the standard. No coherent change was observed after stimulating over right AG or left and right SMG. The authors concluded that these results underline the importance of the AG in representing numerical magnitude. It is not clear, however, why this effect was absent in a control experiment (Experiment 3). This experiment differed from the main experiment (Experiment 1) only with respect to the response hand assignment, i.e. the mapping of the larger/smaller decision to the manual responses was reversed. Furthermore, in a recent review of fMRI-studies on number processing Dehaene et al. (2003) have pointed out the importance of the hIPS for magnitude representation rather than the AG. Therefore, the assumption that the AG plays a pivotal role for number comparison is equivocal.

Sandrini, Rossini and Miniussi (2004) stimulated posterior parietal cortex via high-frequency rTMS (15Hz). Participants were asked to indicate on which side of the screen the larger of two one-digit numbers was presented. Results revealed main effects for the factors (i) stimulation site and (ii) numerical distance, indicating that participants responded more slowly (i) when rTMS was applied to left posterior parietal cortex (IPPC) as compared to the homologous right hemispheric site (rPPC) or sham stimulation, and (ii) when numerical distance was small. The distance effect
appeared to be modulated by rTMS: It was somewhat larger under IPPC stimulation compared to
rPPC or sham stimulation. However, this interaction was not statistically reliable. The absence of a
significant impact of rTMS on the distance effect might be attributable to the actual stimulation
parameters (15Hz for 225 ms). That is, the facilitating effects of 15Hz online (i.e. accompanying the
cognitive task of the participants) stimulation might not be ideally suited to effectively influence
cognitive effects as robust as the numerical distance effect. The impact of rTMS is related to the
number of pulses administered, which is limited for reasons of security in a high-frequency rTMS
paradigm (Wassermann, 1998). Moreover, online rTMS paradigms suffer from attentional
distraction due to side effects of the stimulation (e.g. noise or discomfort; Pascual-Leone, Bartres-
Faz, & Keenan, 1999).

More recently, Andres and colleagues (Andres, Seron, & Olivier, 2005) have used single
pulse TMS to investigate the involvement of the posterior parts of the IPS in number comparison.
TMS pulses were delivered over left and right PC, either unilaterally or bilaterally, while participants
were engaged in a single digit number comparison task with a fixed standard (5). Sham stimulation
was used as a control. The timing of the TMS pulses was varied: Stimulation could occur 150, 200,
or 250 ms after digit presentation. Most importantly, reaction times increased in trials with a small
numerical distance (1 and 2) from the standard with unilateral TMS over the left PC and bilateral
TMS over both hemispheres. With bilateral TMS, trials with a large numerical distance were
responded to more slowly, too. The results in conditions with sham stimulation and unilateral
stimulation of the RH did not differ from each other. According to the authors, these results imply a
lateralization of numerical competence with the LH being involved in precise coding of numerical
magnitude while the RH is limited to approximate numerical judgements. Authors propose that this
differentiation emerges from the link between (finger) counting strategies and language processes
in the LH. What remains unclear is why the results were not modulated by the timing of the TMS
pulses.

1.1.2.2 Neural Correlates of Two-Digit Number Processing

In a recent fMRI study, Wood, Nuerk and Willmes (2006) used parametric regressors to
investigate the neural correlates of decade distance and signed unit distance. The signed unit
distance (negative for incompatible and positive for compatible number pairs) served as a
parametric measure of the amount of unit-decade compatibility. This parametric analysis allowed a
detailed analysis of two important components of two-digit number magnitude comparison. Decade
distance bilaterally activated posterior aspects of the IPS and additionally activated an area in the
right anterior part of the IPS (Talairach Coordinates (TC): 40, -38, 34). Unit distance, on the other
hand lead to increased activity in anterior portions of the IPS (TC: 44, -37, 42). A conjunction
analysis revealed two focal activations in the right IPS, one in the anterior part of the IPS (TC: 44, -
37, 46) and one located more posterior (TC: 40, -51, 58). Wood and coworkers (Wood, Nuerk, et al., 2006) argue that while both right aIPS and bilateral posterior portions of the IPS (pIPS) are recruited in computing position and magnitude of the relevant decade digit, only the right aIPS captures the interaction between decade and unit digit magnitude. That is, this region is activated by the semantic interference between unit and decade digit magnitude. Therefore, the results of Wood and colleagues are consistent with the view that the aIPS in the right hemisphere is associated with integrating stimulus features from different dimensions. Taken together, these results suggest that the aIPS is involved in the integration of unit-decade magnitude information.

1.1.2.3 Differential Involvement of Both Hemispheres

Recently, Ratinckx and colleagues (Ratinckx, Nuerk, van Dijk & Willmes, in press) used visual half field presentation to investigate the differential involvement of both hemispheres in the process of two-digit magnitude comparison. Number pairs which were presented to the left visual field (LVF) and are therefore initially projected to the right hemisphere (RH) show a reduced compatibility effect as compared to number pairs presented to the right visual field. The reduced compatibility effect may be due to a more holistic processing style of the RH: If the RH relies more strongly on overall magnitude in the process of two-digit magnitude comparison than on decomposed unit- and decade magnitude representations the compatibility effect must be reduced, because overall distance was equal for compatible and incompatible number pairs. The mere presence of a compatibility effect in both half-field conditions, however, implies relative rather than absolute differences in processing styles of both hemispheres.

Evidence from case reports of brain-damaged patients also supports the assumption of a strong impact of the left hemisphere (LH) in processing decomposed unit- and decade magnitude representations. Two patients with left-hemispheric lesions have been reported who were particularly impaired in transcoding tasks with multi-digit numbers (Lochy, Domahs, Bartha & Delazer, 2004; Grana, Girelli & Semenza, 2003). The transcoding difficulties were associated with the process of decomposing spoken multi-digit numbers into the constituting digits and the appropriate use of syntactic rules inherent in the Arabic number system. This implies that the impaired brain areas in the LH are important for decomposed magnitude processing. Note that in both patients magnitude comparison of multi-digit numbers was intact. However, this may as well be accomplished with recourse to the analogue overall magnitude representation. It would be interesting to test these patients with a stimulus set which provides the possibility of disentangling the use of different magnitude representations, i.e. decomposed and holistic representation.

Taken together, it appears reasonable to assume hemispheric differences in terms of analogue or decomposed magnitude processing, akin to the differences reported from the domain of vision (e.g. Fink et al., 1996). Based on the original findings of Navon (1977), in an fMRI study
Fink and colleagues found that the left hemisphere was relatively more involved than the right hemisphere in the processing of local information rather than the overall, global form of a visual stimulus. The opposite was true for the RH which was more active when participants had to process the overall shape of the object.
1.1.3 Models of Number Processing

In this section, three models of number processing will be briefly described. The fact that these models disagree on some major issues, which some of the experiments have been concerned with, makes them highly significant for this thesis. The most central issue the three models disagree on is the nature of the mental number representation. This will be the focus of this section.

1.1.3.1 Dehaene’s Triple Code Model

Dehaene and colleagues (e.g. Dehaene et al., 2003) have proposed a theoretical framework which proposes that numbers are represented in three different codes: analogue, visual and auditory (see Figure 2). The auditory number representation is used for the retrieval of rote arithmetic knowledge, such as multiplication tables. Dehaene and Cohen (1995) describe this code as a “verbal word frame, in which numbers are represented as syntactically organized sequences of words” (p. 85). It engages left hemispheric perisylvian areas and the angular gyrus, basal ganglia and thalamic nuclei. The visual Arabic code represents numbers as strings of digits. It is situated within the ventral stream (cf. Ungerleider & Mishkin, 1982) and the adjacent occipito-temporal junction, bilaterally. Both auditory code and visual code do not automatically access the numerical magnitude information. Instead, these number representations are asemantic and symbolic. The third code is the analogue magnitude representation. Here, the numerical magnitude or quantity of a number is retrieved.

Figure 2: Simplified diagram of the Triple-Code model (Dehaene & Cohen, 1995).
The mental representation of numerical magnitude may be best described by the term ‘mental number line’. This mental number line appears to be spatially oriented from left to right (Dehaene, et al., 1993; Fias et al., 1996; Fischer, Castel, Dodd, & Pratt, 2003; Nuerk, Iversen, & Willmes, 2004; Nuerk, Wood, & Willmes, 2005) and to be logarithmically compressed (e.g. Dehaene, 2003). This representation is thought to rely on areas around the horizontal part of the intraparietal sulcus (hIPS), bilaterally. These areas are activated whenever numbers are perceived or processed, irrespective of notation or conscious processing (e.g. Naccache & Dehaene, 2001; Delazer et al., 2003). The bilateral hIPS are the main candidate areas for neural correlates of the mental number line. Figure 3 shows the postulated representations superimposed on an exemplary brain. For the upper left part of the image, the brain is depicted as though looking down from above with the nose being at the top of the image. The left hemisphere appears on the left side of the image. For the other parts, the brain is depicted as though looking from the left side, with the nose at the left side of the image. Skin and bone have been removed using Localite® software (http://www.localite.de).

Hubbard and colleagues (2005) have recently developed a differentiation of the specific parietal structures and their involvement in number processing. Most importantly, they postulate that the interaction between lateral and ventral intraparietal regions (lIP and vIP) is most important for number processing. The area lIP is postulated to mediate shifts along the mental number line by shifts of attention, very similar to attentional shifts in the external world. Area vIP is thought to be involved in the more basic coding of (numerical) quantity. Since “hIPS” is the more generic term and widely accepted as being crucially involved in numerical magnitude processing, this term will be used throughout this thesis.
Figure 3: Anatomic grey-matter correlates of the Triple-Code model: Green: horizontal aspects of the intraparietal sulcus in a top-view on parietal cortex; Turquoise: language areas in the left hemisphere; Yellow: visual number form area in the occipito-temporal junction in the left hemisphere; Red: angular gyrus
1.1.3.2 McCloskey's Model of Number Processing

The central claim of McCloskey's cognitive architecture (McCloskey, Caramazza, & Basili, 1985, see Figure 4) is that there is one central semantic representation which codes the quantity of a given number and that this central representation is accessed by all input formats, regardless of the required output. According to this model, the central representation reflects the structure of the base-ten system. The two-digit number “47”, for instance, would be represented as \(\{4 \times 10^1, 7 \times 10^0\}\). This implies that the input representations do not carry any quantity information as such, but only access the central semantic representation.

The postulate of a mandatory access of all numbers to the central magnitude representation leads to interesting predictions. That is, when participants are given an Arabic number with the task of reading it out aloud, this automatically and inevitably requires accessing the central semantic number representation and activating the numerical magnitude of the given number. Therefore, transcoding without comprehending the numerical magnitude of a number is not possible.

![Figure 4: McCloskey's (McCloskey et al., 1985) model of numerical cognition and transcoding. Note that irrespective of the modality all inputs mandatorily accesses the abstract internal magnitude representation.](image-url)
1.1.3.3 The Hybrid Model by Nuerk & Willmes

The model of Nuerk & Willmes deals primarily with two-digit magnitude comparison. With respect to the nature of the number representation it can be regarded as a trade-off between the assumption of an analogue magnitude representation (Dehaene and colleagues) and a decomposed way of representing numerical magnitude (McCloskey and coworkers). That is, according to Nuerk and Willmes the representation of a two-digit number contains three (interacting) levels: An overall magnitude representation akin to the Triple-code model of Dehaene, and two decomposed magnitude representations for decade and unit digit magnitude, akin to the model of McCloskey. Unlike in the model of McCloskey, the hybrid-model of Nuerk and Willmes postulates that unit and decade digit representations carry semantic meaning (i.e. numerical magnitude) themselves, instead of being merely symbolic representations.

In the course of a two-digit magnitude comparison task, all three representations of the two number involved are compared to each other. That is, the unit digits are compared to each other, the decade digits are compared to each other, and the overall magnitude of both numbers is compared. If these comparison processes lead to divergent results the response latency increases. For example, when comparing 62 to 47 the overall magnitude comparison (62 > 47), decade digits comparison (6 > 4) and the comparison of the unit digits (2 < 7) result in different response tendencies. This conflict will result in increasing response latencies. Figure 5 shows the model framework by Nuerk and Willmes (2005).

\footnote{Note that according to Wood, Mahr and Nuerk (2005), even the constituting digits of a two-digit number are compared to each other despite this comparison process being meaningless for the task at hand.}
Figure 5: The model framework for two-digit number magnitude comparison by Nuerk and Willmes (2005)
1.1.4 The Role of the hIPS in Other Cognitive Domains

Although integrating single digits into one multi-digit number is central for number processing and the symbolic number system, the neural basis of this integration has rarely been studied. As laid out before, this integration process in the Arabic place-value system requires both: (i) spatial (place) encoding of a given digit’s position within a multi-digit number and (ii) the representation of its numerical value according to its position. Parietal cortex subserves a set of processes presumably involved in this integration: Firstly, it is involved in spatial processing (e.g. Kosslyn, 1994). Especially the coding of location information is a well known function of parietal cortex (Haxby, Grady, Horwitz et al., 1991). Secondly, parietal cortex subserves both orienting attention on the basis of either location related (Fan, McCandliss, Fossella, Flombaum, & Posner, 2005; Kincade, Abrams, Astafiev, Shulman, & Corbetta, 2005) or object-based information (Arrington, Carr, Mayer, & Rao, 2000). Finally, the hIPS has been shown to be activated bilaterally by tasks requiring the use of viewer-, object-, and landmark-centred information in spatial judgments (Committeri et al., 2004). Therefore, this area is a principal candidate area for the integration of several streams of numerical information into an integrated two-digit number representation. If this integration is disturbed, then the attribution of a value to a certain (decade or unit) digit may be impaired because their position in the Arabic place–value system will then not be as easily identified and consequently less well associated with a numerical value. For two-digit number comparison, this would imply that if decade magnitude and unit magnitude cannot be distinguished well, unit digit magnitude comparisons should produce greater interference when they lead to a response that is different from the relevant decade digit magnitude comparison. This would result in a larger compatibility effect.

Indeed, there is some evidence from fMRI studies that PC is involved in these processes: For single-digit numbers Pinel and colleagues could show that the interference between comparative judgments concerning numerical and physical magnitude can even be predicted from the amount of overlapping fMRI-activity in the hIPS (Pinel et al., 2004): According to this size congruity effect, comparing two numbers with regard to their numerical magnitude becomes more difficult when numerical and physical comparisons lead to diverging results (e.g. 2_9). This implies that both magnitude codes (physical and numerical magnitude) rely on overlapping brain circuits within the parietal cortex. Thus, both seem to interact with each other at a neural level. The hIPS is not only subserving numerical or physical magnitude processing. It also seems to be involved in non-symbolic magnitude processing, such as comparison of line lengths or angles (Fias et al., 2003), as well as estimating time-related information (Walsh, 2003).

Evidence from other domains of cognitive neuroscience supports the view that the IPS plays a role in integrating contradicting stimulus information. A variety of experimental paradigms elicits semantic interference similar to the interference underlying the compatibility effect (see above).
Generally speaking, interference occurs whenever two or more aspects of a given stimulus (or stimulus display) lead to diverging responses or are semantically ambiguous/contradictory. In the Eriksen flanker paradigm for instance, participants are instructed to attend to a central stimulus (e.g. the letter “H”) which is flanked by other letters (e.g. the letter “F”, thus resulting in e.g. “FHF”). The flanking letters have to be ignored and only the central stimulus has to be responded to. When central and peripheral stimuli would lead to diverging responses, response latencies are larger as compared to situations when flanker and central stimulus are mapped to identical responses (e.g. Eriksen and Eriksen, 1974). In an fMRI study Bunge, Hazeltine, Scanlon, Rosen and Gabrieli (2002) observed left-hemispheric IPS activation in an Eriksen paradigm when contrasting incongruent trials against congruent trials (TC: -34, -60, 34 and -34, -40, 54). The authors discuss this activation in the context of hand-related response representations. That is, the activation of the medial bank of the IPS is reasoned to be “[…] related at least in part to the cue-driven activation of, and attention to, responses associated with the hand” (p. 1567, Bunge et al., 2002).

Another paradigm that is frequently associated with conflict resolution processes is the Stroop-paradigm (Stroop, 1935). In the classical Stroop-paradigm, participants have to name the font colour of a colour word, which denominated the same colour, or a colour different from the font colour (e.g. the word “blue” written in red ink). When the colours are inconsistent participants need more time and commit more errors than in consistent trials. The size congruity effect (Henik & Tzelgov, 1982; see above) can be regarded as a numerical variant of the Stroop-paradigm. However, Fan, Flombaum, McCandliss, Thomas and Posner (2003) failed to find consistent parietal activations in their study comparing different conflict-related paradigms. While there was a reasonable amount of activity in the Stroop task, no parietal involvement in the Eriksen paradigm was observed. One possible explanation for the incoherence of parietal involvement may be the fact that the conflict in Eriksen tasks is based upon incompatible stimulus-response (S-R) associations while the conflict in Stroop-like paradigms is caused by semantic interference. That is, the two conflicting stimulus features are semantically related or share the same semantic dimension rather than being mere response conflicts. Van Veen and Carter (2005) have recently tried to disentangle the different contributions of distinct brain areas to both response and semantic conflicts. They employed a modified Stroop task in an fMRI study. In each trial they presented one of four possible colour words, printed in the colours they denominate (e.g. “red” printed in blue or red colour). Participants were instructed to indicate the colour of a colour word by pressing one of two response buttons (e.g. left index finger for blue and red colour). Semantic interference was induced whenever colour and word were mapped onto the same finger but were different from each other (e.g. “red” depicted in blue). Response interference was induced by presenting a word mapped onto another finger than the colour this word was printed in (e.g. “red” depicted in yellow). Most interestingly, only a semantic conflict between two colours led to bilateral activation of the inferior parietal cortex (TC: -45, -56, 47; 50, -54, 46). The centre of activation was located in the
lateral bank of the hIPS. Therefore, one may assume that the medial bank of the IPS (see above) was not involved in this contrast³.

To sum up, parts of parietal cortex appear to be good candidate areas for the integration of single digit information into one multi-digit number since all necessary information, i.e. spatial information (PPC) as well as magnitude information (hIPS) have been shown to activate parietal areas (for a review see Hubbard et al., 2005). Moreover, a reasonable amount of neural overlap has been shown between the two cognitive functions which are investigated here, i.e. integration of decomposed magnitude processing and holistic, analogue magnitude processing (Wood, Nuerk et al., 2006). Different parts of the parietal cortex seem to be involved in conflict processing. It appears that the lateral aspects of the hIPS in the inferior parietal cortex seem to be involved in semantic conflicts, while medial bank of the IPS may play a role in representing motoric (hand) responses or different response alternatives. The latter function seems to activate areas in the anterior parts of the IPS.

³ Note that this study suffers from a methodological problem: One condition (termed SI: semantic incongruent) enters the presented analyses in two ways: Once as the minuend (SI – CO), and once as the subtrahend (RI – SI). This inevitably leads to non-overlapping patterns of activation.
1.1.5 Numbers and Verbal Working Memory

Numbers are represented verbally and non-verbally, e.g. with regard to their numerical magnitude. Beyond their important role in everyday life, numbers are often utilized as stimulus material in (neuro-)psychological testing. Among other tasks, numbers are employed to assess verbal working memory (WM). It is assumed that only the verbal representation of numbers is activated while neglecting other semantic aspects. WM is defined as the capacity of storing and manipulating information during a short period of time. In the most common working memory model by Baddeley (e.g. 1992) three subsystems are postulated: a central executive, a visuospatial sketchpad, and a phonological loop. The central executive originally was thought to be a limited capacity system “to which all the complex issues that did not seem to be […] specifically related to the two subsystems were assigned” (Baddeley, 2003). In more recent variants of the model it is divided into automatic control versus attentional control. The visuospatial sketchpad is responsible for visual and spatial information like the shape of a stimulus or its location. The phonological loop is concerned with the processing of all kinds of verbal material. It comprises two subsystems: a phonological store, and a rehearsal process. Recently, the episodic buffer has been added to the model to account for problems concerning the interaction of WM with long term memory (Baddeley, 2003).

As this section is focusing on verbal WM, we take a closer look at the code underlying rehearsal and storage within the phonological loop. Serial recall paradigms, in which a list of auditorily presented items has to be rehearsed, reveal an effect of sound similarity: Similar sounding items are less well remembered than phonologically dissimilar items (e.g. Hanley & Bakopoulou, 2003). This finding is taken as an indication of a phonological code within verbal WM. Semantic similarity, on the other hand, does not seem to be important (Baddeley, 1966). However, more recent studies did find significant impact of semantic similarity on the irrelevant speech effect thus speaking against the notion of a purely phonological code in vWM: Neely and LeCompte (1999) found that irrelevant speech containing strong free associates disrupted serial recall more than unrelated irrelevant speech or pure noise did. To date the role of semantics in vWM is still under debate.

In addition to “classical” methods of verbal WM assessment like digit span tasks, new paradigms have been proposed, that rely entirely on the numerical meaning of digits (MacDonald, Almor, Henderson, Kempler, & Andersen, 2001). Specifically, participants have to reorder a list of numbers according to their numerical magnitude. Given the strong activation of semantic magnitude in all kinds of number processing tasks (e.g. Naccache & Dehaene, 2001) it is hard to conceive that these tasks measure only verbal working memory.

Numbers differ from other verbal materials (e.g. letters) in many ways. Numbers have several semantic properties such as numerical magnitude, parity or multiplicativity (e.g. Dehaene et al.,
1993a; McCloskey & Macaruso, 1995). Most important for our purpose is the numerical meaning of numbers. In one influential model (Dehaene et al., 1993) the mental representation of numbers is described by the metaphor of the mental number line. Perceiving numbers automatically activates the mental number line irrespective of the semantic dimension the task refers to (e.g. Dehaene et al., 1993b; Greenwald, Abrams, Naccache, & Dehaene, 2003). For instance, in a physical size comparison task numerical magnitude information interacts with the physical size of numbers (Henik & Tzelgov, 1982; Schwarz & Ischebeck, 2003) suggesting a common representation that is accessed by both properties.

Numbers have also been shown to activate spatial associations (e.g. Baechtold, Baumuller, & Brugger, 1998; Fias et al., 1996; Fischer et al., 2003; Nuerk et al., 2002). In particular, in a parity judgment task small numbers are responded to faster with the left hand while large numbers elicit faster responses with the right hand (SNARC effect: Spatial Numerical Association of Response Codes). This is thought to be due to a(n) (in)congruency of the responding hand with a spatial representation of numbers along a mental number line that is oriented from left to right (Dehaene et al., 1993). Zorzi, Priftis and Umilta (2002) have reported on patients suffering from representational neglect whose error pattern in a numerical bisection task is very similar to the behaviour shown in spatial bisection tasks: When asked to bisect a numerical interval, these patients show a systematic misplacement of the numerical middle to the right. According to the authors spatial aspects of the mental number line bear a close resemblance to physical lines.

This raises the question whether numbers can be regarded as a good operationalisation of verbal stimulus material in order to assess verbal WM. Two caveats emerge from the reported results. First, automatic access of numerical magnitude, i.e. a verbal semantics, casts some doubt on the claim that information processing within the phonological loop is solely phonological as proposed by Baddeley (1966, 2003).

Second, as the representation of numbers apparently possesses spatial and semantic magnitude attributes (Dehaene et al., 1993a) one might question the purely verbal character of numbers when verbal WM is assessed.

Apart from asking whether numbers should be employed in the assessment of vWM there is growing interest in the anatomical mapping of cortical functions like WM within the brain. However, if the mere presentation of numbers automatically activates a verbal semantic representations (i.e. magnitude representation or spatial representation), irrespective of the task, the question arises about a specific contribution of numbers in WM imaging studies: WM has repeatedly been associated with a cortical network comprising parietal (PC) and prefrontal (PFC) cortex as well as the anterior cingulate (AC), supplementary motor and premotor areas (e.g. Jonides, Schumacher, Smith, Koepppe, Awh, et al., 1998).

The impact of different PFC areas with respect to Baddeley’s WM model has been discussed controversially. On the one hand, there is evidence in favour of separate roles for ventrolateral and
dorsolateral prefrontal cortex (VLPFC and DLPFC, respectively) according to the stimulus material being processed, both from primate studies (Levy & Goldman-Rakic, 2000 for a review) and functional imaging studies with humans (e.g. Haxby, Grady, Ungerleider, & Horwitz, 1991; Sala, Raemaekers, & Courtney, 2003; but see Nystrom, Braver, Sabb, Delgado, Noll et al., 2000). On the other hand an organization-by-processes principle has been proposed. While some authors differentiate between phonological and semantic processing (Poldrack, Wagner, Prull, Desmond, Glover et al., 1999) others favour a distinction between manipulating and maintaining (D’Esposito, Postle, Ballard, & Lease, 1999; but see Veltman, Rombouts, & Dolan, 2003). To sum up, evidence for the role of PFC in WM is equivocal so far. But one can at least state that in the context of WM tasks activation within PFC seems to be modulated by both task and stimulus material.

More conclusive are studies about the role of PC in WM. Most of the activations observed are interpreted in terms of phonological storage processes (Awh, Jonides, Smith, Schumacher, Koeppel et al., 1996; Becker, MacAndrew, Danean, & Fiez, 1999; Jonides et al., 1998). Also, processing of order information in WM contexts is thought to rely on PC (Marshuetz, Smith, Jonides, DeGutis, & Chenevert, 2000; Marshuetz, 2005). PC is involved in many different tasks, however. Functions as diverse as mental rotation (Alivisatos & Petrides, 1997), mental size transformations (Larsen, Bundesen, Kyllingsbaek, Paulson, & Law, 2000), and (spatial) attention (e.g. Astafiev, Shulman, Stanley, Snyder, Van Essen et al., 2003) evoke parietal activity.

Additionally, parietal contributions are also consistently found in number processing tasks (Chochon, Cohen, van de Moortele, & Dehaene, 1999; Pinel et al., 1999; but see Shuman & Kanwisher, 2004 for contradicting evidence). Simon, Mangin, Cohen, Le Bihan and Dehaene (2002) tried to subdivide parietal cortex with respect to different tasks including grasping, pointing, saccades, attention, calculation and phoneme detection. Most importantly, calculation (i.e. subtracting presented digits from a given standard) resulted in a stronger activation in a part of the IPS mesial to the SMG compared to other tasks also tapping parietal functions. Activation of hIPS was also found by Eger, Sterzer, Russ, Giraud and Kleinschmidt (2003) who have claimed that hIPS activity is stimulus-driven and number-specific. In contrast, Fias and colleagues (2003) tried to generalize the involvement of IPS from numbers to more concrete/non-symbolic quantity representations like line length or angles. In their study, participants had to compare two lines with respect to their length, two numbers with respect to their magnitude and two angles with respect to their aperture. In a conjunction analysis the authors found the IPS to be jointly activated in all three tasks, suggesting some neural overlap of quantity representation between symbolic and non-symbolic stimuli. In a recent review, Dehaene and coworkers (2003) meta-analyzed several studies from the field of number processing and proposed that the hIPS subserves the core quantity system being “analogous to an internal ‘number line’ “(p. 487) which can be supplemented by two separate systems: (i) a system for manipulation of verbal numbers, i.e. left angular gyrus, and (ii) bilateral posterior superior parietal lobes (PSPL). The latter are claimed to be responsible for attentional...
aspects similar to attentional orienting in space, i.e. shifting attention along the mental number line is comparable to attention shifting in space. Beyond automatic activation of the hIPS simply due to the presentation of numbers, Dehaene and his coworkers (2003) also postulate that activity in the hIPS is increased whenever context explicitly requires processing of magnitude information.

Not only associations between numerical magnitude and space have been reported, but also association between other ordinal sequences and space. The SNARC effect (see above) has not only been observed with numbers but also with letters or months (Gevers, Reynvoet, & Brysbaert, 2003). This seems to suggest that letters share at least some major properties with the numerical dimension in that some magnitude or sequence representation is activated automatically and associated with space. Therefore, Dehaene’s postulate that activity in the hIPS is increased whenever number magnitude is processed might be transferred to processing other ordinal sequences such as alphabetical position of a letter.

Note that Dehaene’s analyses do not necessarily imply that there is a category-specific and exclusive hIPS activation linked by a one-to-one mapping to numerical magnitude. However, they make a strong point that if a number magnitude representation is involved this may lead to stronger hIPS activation as compared to other parietal tasks.

To sum up, number processing seems to rely on the hIPS and other parietal areas, some of which are distinct from those found in WM tasks but some do overlap. Most interesting, like PFC activation in WM tasks is modulated by task and/or stimulus material the same seems to hold for parietal activity in different contexts.
1.2 A Brief Outline of the Experiments of the Current Thesis

This thesis is divided into two parts. The first part is concerned with the mental representation of numbers. It elaborates the structure and neural correlates of the mental representation of two-digit numbers and the process of integrating unit and decade magnitude information into a coherent two-digit number representation. It contains 3 Studies (Study 1 to Study 3) with a total of 5 Experiments. The second part deals with the question whether a hypothesized automatic activation of numerical magnitude information significantly influences the results in the assessment of verbal working memory. Therefore, both the stimulus material and the task were manipulated in order to investigate how these factors (and their interaction) modulate the outcome in an n-back task. Study 4 constitutes the second part of this thesis.

In Study 1, the structure of the mental representation of two-digit number magnitude was investigated. The holistic approach (cf. Dehaene et al., 1990) was tested against the postulated decomposed magnitude representation (cf. Nuerk & Willmes, 2005). Study 1 contains three RT-experiments:

The main objective of Experiment 1 was to inquire whether the unit distance and unit-decade compatibility effects obtained by Nuerk et al. (2001) get affected differently by SOA or not (cf. Dehaene et al., 1990). Such differences would be strong evidence that decades and units are indeed processed separately in two-digit number comparison. Therefore, we extended the SOA range used by Dehaene and colleagues (1990) in a two-digit number magnitude comparison paradigm using the stimulus set of Nuerk and colleagues (2001).

Experiment 2 was designed to test the influence of attentional biases on the performance in two-digit number magnitude comparison. In Experiment 1, the numbers always appeared on the same on-screen position. Additionally, the mask which was used indicated in 100% of the trials, where the relevant information would appear. That is, participants tried to focus their attention on the left-most column of digits and tried to ignore the unit digits. This might result in a mitigated influence of unit-digit magnitude on the overall magnitude comparison process. Therefore, we introduced a second class of stimuli in Experiment 2. 50% of the trials now contained two-digit numbers from the same decade (within-decade trials). This should thwart any strategy of concentrating on the decade digits only, because within-decade trials can only be responded to correctly when the unit digits are taken into account.

Experiment 3 was designed to complement Experiment 2. In Experiment 2, we tried to counteract any attentional biases favouring the decade digits over the units by varying the stimulus set. In Experiment 3, we modified the experimental procedure of Experiment 1. We jittered the on-screen position of the two-digit number slightly on a trial-by-trial basis. In trials with an SOA ≠ 0, the
first digit of each two-digit number simultaneously appeared in the middle of the screen. However, in these trials, the second pair of digits appeared to the left in 50% of the trials whereas in the other half of the trials the second pair of digits appeared to the right. Therefore, participants could never focus their attention on a certain point in space (the position where the decade digits would appear in Experiment 1). Rather, participants now had to determine in each trial whether the digits appeared first represented the units or the decades.

Study 2 was designed to investigate the neural representation of two-digit number magnitude comparison by means of fMRI. A recent fMRI study (Wood et al., 2006) suggests a numerotopic organization of the IPS, i.e. a differential neural activation of decade and unit information. Study 2 extends the study of Wood and coworkers who have used a stimulus set that consisted exclusively of number pairs from different decades. Here, between-decade trials were introduced to increase the salience of the unit digits which in turn results in a larger amount of semantic conflict in the two-digit number magnitude comparison task used.

Study 3 complements Study 2 by reversing the role of the neural activity in parietal cortex. In Study 2 the neural activity was measured by the observed changes in Blood Oxygenation Level Dependent (BOLD) signal acted as the dependant variable. In Study 3, rTMS was used to induce a virtual lesion in the left parietal cortex. Thus, we modified the neural activity of circumscribed brain regions and investigated to what degree this would affect numerical cognition. Performance of participants in a two-digit number magnitude comparison task was analyzed. The cognitive effects under scrutiny, i.e. compatibility effect and distance effect served as indices for the processes of (i) integrating (conflicting) unit and decade magnitude information and (ii) processing of numerical magnitude per se. If the stimulated brain areas are crucially related to the functions captured by the cognitive effects, a change in these effects would imply a functional necessity of the stimulated brain structures for the respective cognitive process.

Study 4 was concerned with the question whether numbers are good candidates to serve as stimulus material in assessing verbal working memory (vWM). Although numbers carry a verbal semantics (i.e. magnitude) they are often utilized in verbal working memory tasks. However, vWM is thought to rely on a purely phonological code. Here we tested the influence of (i) a verbal semantics and (ii) different tasks on performance in a vWM context by examining stimulus and task specific variation of activity in the horizontal parts of the hIPS. The hIPS has previously been shown to subserve magnitude processing modulated by (i) specific stimuli and (ii) specific tasks. If we observe any semantic influences of numbers on the verbal working memory performance, this would mitigate the possibility of interpreting results from verbal working memory assessment comprising numerical stimuli as being purely verbal in nature. Rather, semantic influences would have to be taken into consideration as well. To this end, we employed 2 variants of the n-back task either with letters or with numbers as stimuli while recording changes in cortical blood flow by fMRI.
2 Study 1:

Is Numerical Processing Analogue? How Decomposed Two-Digit Number Processing can be Affected by Strategy

Experiments 1 and 2 are submitted for publication
(Co-authored with H.-C. Nuerk and K. Willmes)
2.1 Experiment 1

The main objective of Experiment 1 was to examine whether the unit distance and unit-decade compatibility effects obtained by Nuerk et al. (2001) get affected differently by SOA or not (cf. Dehaene et al., 1990). Such differences would be strong evidence that decades and units are indeed processed separately in two-digit number comparison.

To detect the time course of unit-specific interference effects more comprehensively, we used 4 SOAs [50ms, 100ms, 200ms, 400ms] in which the decade digits appeared before the unit digits and another 4 symmetrical SOAs (i.e., also [50ms, 100ms, 200ms, 400ms]) in which the unit digits appeared before the decade digits. In addition, one simultaneous condition served as a control condition in which all digits of the two two-digit numerals appeared together. We defined the SOAs to be negative when the decade appeared first (e.g. for SOA = -200 the decade digits appeared 200ms earlier than the unit digits) and to be positive SOAs when the units appeared first.

Hence, the central question in this study is: Do unit-specific interference effects differ for different SOAs? If the results of Dehaene and colleagues are replicated, we would find null effects, however, if the unit-specific interference is due to separate processing (cf. Dehaene et al., 1990; and outline of the argument above), we should expect larger unit interference effects when the units appear first. This central question is qualified in two respects: (i) Stimulus-specificity: We have argued that the null SOA effect found by Dehaene and colleagues may be due to their particular stimulus choice leading to only small unit distances. If this argument is true, the interaction between SOA and compatibility should be modulated by unit distance. (ii) Time course-specificity: Dehaene and colleagues examined SOAs of [-50, 0, 50]. However, 50ms may be too short to modulate decade or unit activation patterns significantly. Therefore we extended the SOA range to a maximum of 400ms.
2.1.1 Methods

2.1.1.1 Participants

24 volunteers (12 men; mean age: 27 years) participated in the experiment. They all had normal or corrected to normal vision and all but two were right handed according to the Edinburgh Handedness Inventory. They received 11 € after the experiment. Three participants were discarded from the sample because of either not following the instructions (1) or showing an overall error rate higher than 10% (2).

2.1.1.2 Stimuli and Design

The same stimuli as in Nuerk et al. (2001) were used: 240 different two-digit number pairs between 21 and 98 were presented in a 9 X 2 X 2 X 2 within-participant design comprising the following factors: stimulus onset asynchrony of decades and units (-400ms, -200ms, -100ms, -50ms, 0ms, 50ms, 100ms, 200ms and 400ms; negative times indicating the earlier appearance of the decade digit), decade distance (small: 1 - 3 vs. large: 4 - 7), unit distance (small: 1 - 3 vs. large: 4 - 8), and compatibility (compatible vs. incompatible, see above). Overall distance, decade distance, unit distance, and problem size were all matched both, absolutely and logarithmically, between the respective stimulus groups (except for the overall distance varying necessarily with decade distance, see Nuerk, Weger et al., 2001, 2004). We decided to keep the decade distance manipulation from the stimuli of Nuerk et al. (2001), because in some studies compatibility effects were obtained in particular for small decade distances, but less so for large decade distances.

2.1.1.3 Procedure

The experiment was run on a 1.6GHz-PC. Participants sat approximately 50cm from the screen in a dimly lit room. The stimuli were presented on screen above each other using “Arial” font. A single digit extended to 1.2° vertical angle and 0.8° horizontal angle.

Participants were instructed to indicate which number was numerically larger by pressing the corresponding key with their right (top key) or with their left index finger (bottom key). The participants were instructed to respond as soon as possible. Response keys were located above each other – congruent with stimulus arrangement.

Each trial began with the presentation of a blank screen for 200ms followed by a mask which consisted of one cardinal sign in each digit position. After 300ms, the mask was replaced by the first two digits (decades or units of the two different numbers). The remaining two digits followed after the specified SOA. In trials with simultaneous presentation of both digits of a number (i.e., also with simultaneous presentation of both numbers), the mask was replaced after 300ms.

Each session started with an instruction which was followed by 10 practice trials with random SOAs. The experiment consisted of nine blocks of 240 trials each which the participant initiated via
a key-press. SOAs were presented in pseudo-randomized order. Each block contained all 240 stimuli with randomly chosen SOAs. Trial and SOA sequence was pseudo-randomized for each participant individually.

RT measurement started with the appearance of the decade digits. This way of RT measurement was chosen, because theoretically, decade digits convey sufficient information to solve the task (cf. Dehaene et al, 1990).

The whole experimental procedure lasted approximately 75 minutes, depending on how long participants rested between blocks.
2.1.2 Results

RT analysis was based on correct trials only (total error rate: 3.87%). The trimming procedure excluded RTs outside [200, 1400] ms and - in a second step - trials outside 3 SD around a participant’s average RT. A total of 386 (0.85%) RTs fulfilled these criteria and were thus excluded from further analyses. The statistical analysis was chosen in accord with the aforementioned scientific hypotheses to be tested (cf. Hager, 2002). We first report the results from a 9 x 2 x 2 x 2 repeated measures ANOVA with the factors SOA, decade distance, unit distance, and compatibility before we explore the more specific hypotheses. A full overview over all mean RT observed in all conditions can be found in Table 1.

![Compatibility Effect](compatibility-effect.png)

*Figure 6: Compatibility effect (difference between incompatible and compatible trials) for each SOA depicted separately for small and large unit distances in Experiment 1. SOA was coded negatively when the relevant decade digit appears before the unit.*
Table 1: Mean reaction times and mean error percentages in Experiment 1 for all conditions with standard errors in parentheses

<table>
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<tr>
<th>Compatibility</th>
<th>Unit distance</th>
<th>decade distance</th>
<th>SOA (ms)</th>
</tr>
</thead>
<tbody>
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<td></td>
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<td>-100</td>
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<tr>
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<td>759 (30)</td>
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<td></td>
<td>large</td>
<td>small</td>
<td>803 (27)</td>
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<tr>
<td></td>
<td></td>
<td>large</td>
<td>756 (30)</td>
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<tr>
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<tr>
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<td>759 (30)</td>
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<tr>
<td></td>
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<td>small</td>
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<td></td>
<td>large</td>
<td>756 (30)</td>
</tr>
<tr>
<td></td>
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<td>small</td>
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Overall Results

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<th>778 (29)</th>
<th>764 (25)</th>
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<th>741 (20)</th>
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<td>3.61 (.72)</td>
<td>4.54 (.90)</td>
<td>4.27 (.92)</td>
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</table>
2.1.2.1 Analysis over All SOAs and Stimulus-Specificity

The most important finding for this study is that compatibility interacted significantly with SOA in the overall ANOVA (F(8, 160) = 4.58, p < .01, see Figure 6) although there was no indication of a main compatibility effect (F < 1). As we will see below, this interaction is due to the fact that compatibility effect tends to be inverted for negative (decade-first) SOAs and regular for positive (unit first) SOAs. As expected, there was a strong decade distance main effect (F(1, 20) = 508.43, p < .01): Larger distances led to 56 ms faster magnitude comparisons. A small main effect of absolute unit distance also reached significance over the large number of trials (F(1, 20) = 5.65, p < .05): Smaller absolute unit distances were 2 ms faster than larger absolute unit distances. Finally, there was a main effect of SOA (when RT was measured from the onset of the decisive decade digit; F(8, 160) = 21.26, p < .01). There was a strong linear trend (F(1, 20) = 16.51, p < .01, all F-values Greenhouse-Geisser adjusted) such that RT became faster with increasing SOAs. However, this was only true when measured from the onset of the relevant decade digits. If SOA were measured starting with the last digit, RT was actually slowest for simultaneous presentation and about 350 ms faster when the relevant decade digits appeared 400 ms earlier.4

Decade distance interacted with compatibility (F(1, 20) = 4.45, p < .05), and SOA (F(8, 160) = 3.81, p < .01). The compatibility effect tended to be positive for large decade distances and negative for small decade distances. However, these overall interactions were all qualified by SOA. No other interaction reached significance. There were no indications of Speed-accuracy-trade-offs (SATO)s with regard to the compatibility effects. For an overview the full pattern of mean errors is also given in Table 1.

To explore the effect of SOA on two-digit number processing a bit closer, we aggregated the SOA conditions in one negative and one positive SOA condition and explored its interactions. The direction of the compatibility effect depended strongly on SOA (F(1, 20) = 6.20, p = .01). Compatibility effects were small, but regular at positive SOAs (5ms) but reversed at negative SOAs (-5ms). As introduced above, the inverse effect can be interpreted as a decade distance effect. Interestingly, the decade distance effect itself also was 6ms smaller for negative SOAs than for positive SOAs (F(1, 20) = 6.50, p < .05): This finding is interesting because it helps to interpret the inverse compatibility effect. The inverse compatibility effect for negative SOAs could have two reasons: (i) units do not play a strong role, when they appear later or (ii) decades play a stronger role when they appear earlier. The decade distance effect which indexes only the role of the decade digit distances is,

4 Note that any interaction with SOA is not affected in the general linear model by whether SOA is measured from the relevant digit or from the last digit on because all numerical conditions are affected alike by such a transformation.
however, smaller for negative SOAs. Thus, this result indicates, that it is not a stronger role of the decade digits which lead to the inverse compatibility effect for negative SOAs. Rather, the units’ importance seems to be diminished when they appear after the decades.

Finally, there was an important 3-way interaction between units, compatibility and SOA in this analysis ($F(1, 20) = 4.56, p < .05$). The interpretation is straightforward. SOA modulated the compatibility effect for large unit distances ($F(1, 20) = 8.99, p < .01$), while the interaction between (positive or negative) SOA and compatibility was much weaker for small unit distances and failed to reach the conventional significance level ($F(1, 20) = 3.57, p = .07$). Thus, the overall interaction between compatibility and SOA reported above was driven by the results for large unit distances while no significant effect was present for the small unit distances. These small unit distance stimuli were more similar to the stimuli used by Dehaene and colleagues. No other interaction with SOA reached significance in this analysis.

### 2.1.2.2 Time Course-Specificity and Separate Analyses for Short SOAs

The above analyses have shown that (i) SOA modulates unit-decade-specific compatibility effects in a specific way and (ii) this modulation is largely based on SOA modulations for large unit distances. A possible objection is that so far we have analysed the data over all SOAs in the experiment. However, for large SOAs, the decades appeared long before the units, or vice versa. Thus, they might have been viewed as single digits rather than as a two-digit numeral (see Dehaene et al., 1990, for similar arguments). Therefore, we examined how SOA modulated the time course of the compatibility effects for shorter SOAs [-100 <= SOA <= +100] only. Because Dehaene only investigated a subset of these SOAs [-50, 0, 50], we also report the p-values for this subset in parentheses to allow for a comparison with Dehaene’s data. We will see that the overall tendencies do not differ between the two SOA ranges (see also Figure 6), but that the data from Dehaene’s SOA subset are sometimes closer to a null effect, probably due to a lack of power.

Even for short SOAs, the compatibility effect differed already in an ANOVA between the different SOAs ($F(4, 80) = 4.65, p < .01$; for Dehaene’s SOAs $F(2, 40) = 3.24, p = .05$). This difference was due to a linear increase of the compatibility effect in this SOA range (linear-by-linear trend, $F(1, 20) = 8.91, p < .01$; for Dehaene’s SOAs $F(1, 20) = 3.25, p = .08$).

As suggested by Lorch and Myers (1990) and as has become common practice in the investigation of SNARC effects (cf. Fias et al., 1996), we computed a linear regression over the SOAs of [-100, +100] for each participant and for the compatibility effect. The compatibility effects increased linearly from short negative to short positive SOAs ($t(20) = 2.98, p < .01$, mean beta weight: 0.06, i.e., the compatibility effect increased by 6 ms per SOA difference of 100 ms). Considering only the SOAs used by Dehaene and colleagues, the increase in the compatibility effect was slightly more noisy over participants, but...
comparable in size ($t(20) = 1.80, p < .05$, one-tailed, mean beta weight: 0.07, i.e., the compatibility effect increased by 7 ms per SOA difference of 100 ms). As shown in Figure 6, the increase in overall compatibility was mainly due to the effect for large unit distances (for $[-100, 100]$ $t(20) = 3.01, p < .01$, 10 ms per SOA difference of 100 ms; for $[-50, 50]$ $t(20) = 1.85, p < .05$, 10 ms per SOA difference of 100 ms) while for small unit distances no significant effect could be obtained at all (all $p >= .17$, one-tailed).

While modulation of the compatibility effect was reliable across all analyses, the compatibility effect was not. In contrast to previous studies and much to our surprise there was no indication of a compatibility effect for an SOA = 0 ($t = .82, p = .21$, one-tailed). The only regular compatibility effects were observed for short positive (unit-first) SOAs (for 50 or 100ms, both $t(20) >2.18$, both $p < .05$) while these effects disappeared when the unit was presented long before (i.e., 200 or 400 ms, before the decade digit; $p >= .16$, one-tailed).

In sum, the compatibility effect was also systematically modulated by SOA when only short SOAs are examined. The compatibility effect increased linearly with increasing SOA in the range $[-100, 100]$. However, when only small unit distances were examined, we obtained null interactions of compatibility and SOA. When only the SOA range of Dehaene et al. $[-50, 50]$ was examined, we obtained the same trends and interactions as in the range $[-100, 100]$ but a little closer to conventional significance levels. While the modulation by SOA was systematic and reliable over the different analyses and SOA ranges, the compatibility main effects were not. In particular, the compatibility effect at the standard SOA = 0 condition was not replicated.
2.1.3 Discussion

2.1.3.1 Separate Processing of Decade and Unit Magnitudes

The main finding of Experiment 1 is that unit-related effects were strongly modulated by SOA. The unit-decade compatibility effect was larger when the unit was presented first and even inverted when the decade was presented first. This modulation was also found when only shorter SOAs [-100, 100] were explored. When the SOAs of Dehaene and colleagues were used [-50, 0, 50], the trends were the same, but the results were closer to conventional significance levels.

The results also support the hypothesis that the null effects for the different regression slopes reported by Dehaene and coworkers may have relied on the particular (small unit distance) attribute of the stimuli when a fixed standard of 55 is chosen. Apart from decade numbers themselves, compatible or incompatible unit distance was restricted to the range 1-4 (e.g., 39_55, absolute unit distance 9 -5 = 4). However, for our small unit distances (range 1-3) we did not observe any interaction with SOA for the short SOAs which were used by Dehaene and colleagues. Only for larger unit distances, an interaction between compatibility effects and SOA was observed. In this respect, our results actually confirm the findings of Dehaene and colleagues. When unit distances are small, unit-decade compatibility effects are not significantly influenced by different SOAs.

2.1.3.2 Null Compatibility Effect for an SOA of Zero

Although we found compatibility effects and the expected modulation by positive and negative SOAs in this study, we were surprised to find no such compatibility effect with an SOA of zero, which we had used as a control condition. Compatibility effects have been reliably obtained for Arabic numbers (Nuerk et al., 2001), German number words (Nuerk, Weger et al., 2002), Arabic notation in English participants (Nuerk, Weger et al., 2005) as well as with children and adults in other laboratories (Nuerk, Kaufmann et al., 2004; Ratinckx et al., in press) and semi-illiterates (Wood, Nuerk et al., 2006; for a review of compatibility effects, see Nuerk & Willmes, 2005). Hence, the compatibility effect seems to be reliable with simultaneous presentation of decades and units, i.e. with an SOA of zero. So, why did we fail to obtain compatibility effects with an SOA of zero in this study, while compatibility effects for other SOAs [50, 100] were observed in the same participants?

A possible explanation is that attentional processes may have influenced the compatibility effect. We used a similar fixation mask as Dehaene and colleagues (1990) which differed from previous compatibility experiments. The mask consisted of one cardinal sign for each digit position. This mask allowed attending specifically to the location and the object where the relevant decade digit appears as each cardinal sign of the mask was
directly replaced by the respective decade or unit digit. Note that this is an adequate experimental strategy in our study because the unit digit was irrelevant in 100% of the trials (while the unit digit in Dehaene’s study was relevant in about 20% of the trials). Previously, we have never used such a mask which allowed focussing on the exact location of the decade digits (Nuerk, Weger et al., 2001, 2002, 2004; Ratinckx et al., in press; Wood, Nuerk et al., 2006). Thus, previously, no specific visual cue was given which allowed focussing attention so selective on the relevant decade digit.

However, it should be noted that a null compatibility effect for an SOA of 0 does not imply that only the decade digit is processed. When the decade digit would be processed only or predominantly, we should observe an inverse compatibility effect (with incompatible trials being faster) because incompatible trials need to have a larger decade distance than compatible trials when overall distance is matched. Indeed, such an inverse compatibility effect can be observed when the decade digit appears long before the unit digit for negative SOAs but was absent an SOA of 0. Therefore, unit magnitude information must have been processed to a certain extent. This was not sufficient, however, to overcome the inverse compatibility effect which would have resulted from a pure decade digit comparison.

To summarize, while the SOA modulation of the compatibility effect in Experiment 1 was consistent in all analyses, conclusions from an experiment in which the primary effect of interest is not replicated for the standard condition, are equivocal. We therefore tested the attentional hypothesis in a simple way. First, we varied the probability with which the unit digit and the decade digit are informative (Experiment 2). If the unit digit is decisive in 50% of the trials (e.g., in trials like 61_67), it makes no sense to a priori direct attention selectively to the location of the decade digit. If the attentional account is correct, the compatibility effect should reappear with identical perceptual conditions as in Experiment 1 when such trials are included. Second, we changed the experimental procedure in order to prevent participants from concentrating on one pairs of digits only (Experiment 3, see below).
2.2 Experiment 2

The aim of Experiment 2 was to identify the source of the null compatibility effect in Experiment 1 with simultaneous presentation (SOA = 0). Additionally, we wanted to explore whether modulation of the compatibility effect by SOA could be replicated. Since the number of stimuli was doubled by including as many within-decade trials (with the same decade digit, e.g. 61_67) as between-decade trials, the SOA range was restricted to the one used by Dehaene and colleagues [-50, 0, 50].

2.2.1 Methods

2.2.1.1 Participants

12 volunteers (4 men; mean age: 27.7 years) participated in the experiment. They all had normal or corrected to normal vision and all but one were right handed according to the Edinburgh Handedness Inventory. Each participant received 8 € after the experiment.

2.2.1.2 Stimuli and Design

In addition to the identical stimulus set as in Experiment 1, the stimulus set included 240 two-digit number pairs between 21 and 98 from the same decade (within decade trials). 3 SOAs [-50ms, 0ms, 50ms] were used. For within decade trials, unit distance could be either small (smaller than 4) or large (larger than 3).

2.2.1.3 Procedure

The procedure was identical to Experiment 1 except for following variations: In order to minimize time pressure, numbers disappeared after 2000 ms instead of 1400 ms unless a button press terminated trials. Each session started with the instruction which was followed by 20 practice trials (instead of 10) with random SOAs. The experiment consisted of three blocks of 480 trials each initiated by participants via button-press. Different SOAs were presented in pseudo-randomized order, balanced over all three blocks. SOAs were distributed equally across blocks.
2.2.2 Results

As in Experiment 1, RT was measured from the point of time on when participants were able to respond to the stimuli. When the decade numbers appeared first in between-decade trials (54_67), RT was measured from the appearance of the decade digits. In all other cases, participants could only decide when all digits had appeared on the screen. Note that in within-decade trials participants (61_67) could not decide when the unit digits appeared first, because they did not know a priori whether the decade digits appearing later were the same or different. However, please note that in the general linear model, this way of measurement only affects the SOA main effect, but not the other main effects or the interaction with other effects because a constant is added to all conditions alike. RT analysis was based on correct trials only (total error rate 1.98%). The trimming procedure excluded RTs outside 3 SD around a participant’s average RT. A total of 180 (1.04%) RTs fulfilled these criteria and were thus excluded from further analyses.

2.2.2.1 Different Decade Trials

A 3 X 2 X 2 X 2 repeated measures ANOVA for number pairs from different decades comprised the factors SOA, decade distance, unit distance, and compatibility. Main effects were observed for decade distance \((F(1, 11) = 96.24; p < .01, 82 \text{ ms})\), and – most importantly – for compatibility \((F(1, 11) = 52.34; p < .01)\). Participants responded 44 ms faster to compatible as opposed to incompatible number pairs. RT varied with overall SOA \((F(2, 22) = 62.21; p < .01)\): Participants were again slowest when decades appeared first (804 ms), followed by a simultaneous presentation of both numbers (781 ms) and fastest with earlier presentation of units (760 ms; linear contrast: \(F(1, 11) = 98.87; p < .01\), see Figure 7 and Table 2). When RT would be measured from the last digit on in all conditions, overall RT would have reverse U-shape (754, 781, 760 ms, for SOA -50, 0, 50, respectively).
Figure 7: Compatibility effect (=difference between incompatible and compatible trials) for each SOA depicted separately for small and large unit distances. SOA was coded negatively when the relevant decade digit appears before the unit digit and positively when the decade digit appears after the unit digit. Main compatibility effects were observed for all conditions. The compatibility effect decreases with increasing SOAs. The compatibility effect is smaller for small unit distances, but is similarly affected by SOA as for large unit distances.

Compatibility significantly interacted with decade distance (F(1, 11) = 6.46; p < .05) and unit distance (F(1, 11) = 22.32; p < .01). The compatibility effect was larger for the small decade distances than for large decade distances (51 ms vs. 36 ms; t(11) = 2.54; p < .05) which is consistent with results previously obtained for error data (cf. Nuerk et al., 2001; Nuerk, Weger et al., 2005). The compatibility effect was larger for large unit distances as compared to small unit distances (63 ms vs. 25 ms; t(11) = 4.72; p < .01). Note that the inclusion of the within-decade trials led to – at least numerically - larger compatibility effects than in any other study before. No other interaction reached statistical significance. There were no indications of SATOs with regard to the compatibility effects. For an overview the full pattern of errors is also given in Table 2.
Table 2: Mean reaction times and mean error percentages in Experiment 2 for all conditions with standard errors in parentheses

<table>
<thead>
<tr>
<th>Compatibility</th>
<th>Unit Distance</th>
<th>Decade Distance</th>
<th>SOA (ms)</th>
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<td>3.68 (.01)</td>
<td>4.17 (.01)</td>
</tr>
<tr>
<td>large</td>
<td>776 (34)</td>
<td>821 (36)</td>
<td>810 (34)</td>
</tr>
<tr>
<td></td>
<td>1.11 (.00)</td>
<td>.69 (.00)</td>
<td>.69 (.00)</td>
</tr>
<tr>
<td>Overall</td>
<td>802 (37)</td>
<td>842 (38)</td>
<td>836 (36)</td>
</tr>
<tr>
<td></td>
<td>1.77 (.01)</td>
<td>2.19 (.01)</td>
<td>2.43 (.01)</td>
</tr>
</tbody>
</table>
Since the compatibility main effect for simultaneous presentation was the main interest of Experiment 2, we computed the compatibility effect for SOA = 0. With the inclusion of within-decade trials it was clearly significant (t(11) = 5.25; p < .01, 47 ms). Most importantly, the compatibility effect tended to interact with SOA again (F(2, 22) = 2.94; p = .07). A closer examination of this interaction by a linear-by-linear contrast suggested that compatibility linearly decreased with increasing SOA (F(1, 11) = 6.91; p < .05) which was not modulated by unit distance (F < 1). When we computed a linear regression over the SOAs for each participant over the compatibility effect as in Experiment 1, the compatibility effects decreased with increasing SOA (t(11) = 2.45, p < .05, two-tailed, mean beta weight: 0.17, i.e., the compatibility effect decreased 17 ms per SOA difference of 100 ms). The respective regression slopes did not differ between large and small unit distances in Experiment 2.

To summarize, a characteristic modulation of unit effects by SOA was obtained, however, in the opposite direction as in Experiment 1. In contrast to Experiment 1, the compatibility main effect was clearly significant in all analyses.

2.2.2.2 Within-Decade Trials

For pairs of numbers within one decade we computed a 3 X 2 repeated measurement ANOVA with the factors SOA and unit distance. Both main effects were statistically reliable (SOA: F(2, 22) = 45.87; p < .01; unit distance: F(1, 11) = 51.71; p < .01): Participants responded fastest when decades appeared first and the common distance effect was replicated: Same decade number pairs with large unit distance were responded to faster than those with small unit distance (801 ms vs. 851 ms).
2.2.3 Discussion

The analysis of Experiment 2 revealed three important results. First, there were strong compatibility main effects for large and also for small unit distances when within-decade trials were included. Secondly, the compatibility effects were again modulated by SOA in a characteristic way. Finally, however, this modulation was in the opposite direction as in Experiment 1.

In Experiment 1 we could demonstrate a modulation of the compatibility effect by SOA. The null-effect of compatibility for the condition SOA = 0, however, undermines any further conclusions. We discussed an attentional explanation: The mask in Experiment 1 offered the possibility to attend to the location of the decade digits only. However, instead of observing an inverse compatibility effect (see above), we obtained a null compatibility effect.

In Experiment 2 this attentional strategy was tested. The benefit of this strategy depends on the validity of one particular digits’ position for the decision to be made. Thus, if the decade digit position is no longer valid in 100% of the trials, compatibility effect should reappear. Therefore we included 50% within-decade trials in Experiment 2. The results were straightforward. The compatibility effect reappeared and it was numerically stronger than in all previous experiments. This is consistent with the above attentional account. However, it is inconsistent with any general hypothesis that does not take stimulus-induced strategy effects into account and therefore cannot explain the different results in Experiment 1 and 2.

Moreover, Experiment 2 was consistent with Experiment 1 in that there was an SOA modulation of the compatibility effect. It is again inconsistent with the null SOA modulation of unit effects obtained by Dehaene and colleagues as well as with their conclusion that decades and units are holistically processed in two-digit number magnitude comparison. However, the kind of modulation was different in Experiments 1 and 2. This will be dealt with in the general discussion of Study 1.
2.3 Experiment 3

In Experiment 3, a different approach of increasing the salience of the unit digits in a two-digit number magnitude comparison task was chosen. Instead of manipulating the stimulus set (Experiment 2), we used the same stimuli as in Experiment 1. In order to prevent the participants to adopt a strategy of attending ‘only’ to the decade digits, we manipulated the on-screen position of the constituent digits in an SOA experiment: The first pair of digits always appeared in the centre of the screen. However, it was not clear to the participants whether this pair represented decade or unit digits. This became clear only when the second pair of digits appeared – either to the left (decade digits) or to the right (unit digits) of the first pair. Figure 8 schematically depicts one trial. Here the unit digits appeared first.

2.3.1 Methods

2.3.1.1 Participants

30 volunteers (15 men; mean age: 26.2 years, range 19 – 52 years) participated in the experiment. They all had normal or corrected to normal vision and all but one were right handed according to the Edinburgh Handedness Inventory. Each participant received 11 € after the experiment.

2.3.1.2 Stimuli and Design

The stimuli and design were identical to Experiment 1.

2.3.1.3 Procedure

The procedure was identical to Experiment 1 except for following variations: In order to minimize time pressure, numbers disappeared after 1500 ms instead of 1400 ms unless a button press terminated trials. Each session started with the instruction which was followed by 15 practice trials (instead of 10) with random SOAs. The experiment consisted of nine blocks of 240 trials each initiated by participants via button-press. Different SOAs were presented in pseudo-randomized order. The sequence of trials and SOAs was different for each participant. Each stimulus pair appeared with the decade digit first, the unit digit first and with both digits appearing simultaneously. Therefore, negative SOAs indicate the appearance of the decade digits in the centre of the screen, and positive SOAs indicate the central appearance of the unit digits (see Figure 8). The fixation sign differed from Experiment 1. In Experiment 3 we have used a single fixation cross, presented in the centre of the screen for 300 ms.
Figure 8: Schematic depiction of one trial in Experiment 3. Trials began with the presentation of a fixation sign for 300 ms, which was replaced by the first pair of digits presented centrally. Only after the second pair of digits appeared, participants were able to decide on the relative value of the digits within the respective two-digit numbers.
2.3.2 Results

Reaction times were measured from the point of time the complete numbers were presented, since only then participants were able to decide on the identity of the single digits (decades or units).

RT analysis was based on correct trials only (total error rate: 3.87%). The trimming procedure excluded RTs outside [200, 1500] ms and - in a second step - trials outside 3 SD around a participant’s average RT. A total of 1004 (1.55%) RTs fulfilled these criteria and were thus excluded from further analyses. The statistical analysis was chosen in accord with the aforementioned scientific hypotheses to be tested (cf. Hager, 2002). We first report the results from a 9 x 2 x 2 x 2 repeated measures ANOVA with the factors SOA, decade distance, unit distance, and compatibility before we explore the more specific hypotheses. A full overview over all mean RT and error proportions observed in all conditions can be found in Table 3.

Overall ANOVA

A repeated measures ANOVA comprising the factors SOA, decade distance, unit distance and compatibility revealed the following main effects and interactions: Participants responded faster in when decade was small (736 ms) as compared to trials with large decade distance (656 ms; F(1, 29) = 410.29; p < .01). Albeit numerically small, there was an inverse unit distance effect: RTs were smaller with smaller unit distance (693 ms) than with large unit distance (698 ms; F(1, 29) = 31.17; p < .01). Depending on the SOA of units and decades, RTs differed significantly (F(8, 232) = 302.24; p < .01; ε = .288). RTs in the different SOAs followed an asymmetric U-shape, as can be seen in Figure 9.
SOA significantly interacted with decade distance (F(8, 232) = 8.77; p < .01; ε = .989). SOA interacted with compatibility (F(8, 232) = 5.48; p < .01; ε = .992). Compatibility significantly interacted with decade distance (F(1, 29) = 7.89; p < .01). Post-hoc students t-tests revealed that the influence of compatibility was larger in trials with a small decade distance as compared to trials with large decade distance (t(29) = 3.48; p < .01). In trials with a small decade distance a small and inverse compatibility effect failed to reach a conventional level of significance (t(29) = -1.13; p = .27), while for trials with a large decade distance the direction of the compatibility effect was regular, albeit not significant on a conventional Type-I error level (α = .05; t(29) = 1.54; p = .14). The effect of compatibility was also modulated by unit distance (F(1, 29) = 23.50; p < .01). While for small unit distance a significant inverse compatibility effect was observed (t(29) = -2.17; p < .05), no consistent effect emerged for large unit distance (t(29) = 1.47; p = .15). A three-way interaction between compatibility, unit distance and decade distance was observed (t(1, 29) = 5.31; p < .05). No other main effect or interaction was observed. Table 3 gives a comprehensive overview of the RT data in all experimental conditions.
Table 3: Mean reaction times and error proportions for Experiment 3. Standard errors are provided in parentheses.

<table>
<thead>
<tr>
<th>Comp. Unit dist.</th>
<th>Dec. dist.</th>
<th>SOA (ms)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>-400</td>
</tr>
<tr>
<td>Comp.</td>
<td>small</td>
<td></td>
</tr>
<tr>
<td></td>
<td>small</td>
<td>947 (23)</td>
</tr>
<tr>
<td></td>
<td>large</td>
<td>872 (19)</td>
</tr>
<tr>
<td></td>
<td>small</td>
<td>3.33 (.89)</td>
</tr>
<tr>
<td></td>
<td>large</td>
<td>1.56 (.45)</td>
</tr>
<tr>
<td>Overall Results</td>
<td>small</td>
<td>936 (22)</td>
</tr>
<tr>
<td></td>
<td>large</td>
<td>881 (19)</td>
</tr>
<tr>
<td></td>
<td>small</td>
<td>3.44 (.93)</td>
</tr>
<tr>
<td></td>
<td>large</td>
<td>1.87 (.39)</td>
</tr>
<tr>
<td>Incomp.</td>
<td>small</td>
<td>927 (20)</td>
</tr>
<tr>
<td></td>
<td>large</td>
<td>871 (19)</td>
</tr>
<tr>
<td></td>
<td>small</td>
<td>3.54 (.68)</td>
</tr>
<tr>
<td></td>
<td>large</td>
<td>1.35 (.36)</td>
</tr>
<tr>
<td>Overall Results</td>
<td>small</td>
<td>928 (22)</td>
</tr>
<tr>
<td></td>
<td>large</td>
<td>5.10 (.83)</td>
</tr>
<tr>
<td></td>
<td>small</td>
<td>2.71 (.51)</td>
</tr>
<tr>
<td>Overall Results</td>
<td>small</td>
<td>903 (22)</td>
</tr>
<tr>
<td></td>
<td>large</td>
<td>2.86 (.37)</td>
</tr>
</tbody>
</table>
In accordance to Experiment 1 we analyzed the interaction of unit- and decade distance, compatibility and SOA by summarizing over negative SOAs and positive SOAs. Again, the direction of the compatibility effect depended strongly on SOA ($F(1, 29) = 8.71, p < .01$). Compatibility effect failed to reach a conventional level of significance for positive SOAs (2.5 ms; $t(29) = 0.72; p = .48$) and reversed at negative SOAs (-6 ms; $t(29) = -2.28; p < .05$). As introduced above, the inverse effect can be interpreted as a decade distance effect. Compatibility interacted with unit distance: While for small unit distances a negative compatibility effect emerged (-6.6 ms; $t(29) = -2.97, p < .01$), a numerically regular, albeit non-significant compatibility effect (3 ms; $t(29) = .84; p = .41$) was observed for large unit distances. Compatibility interacted with decade distance ($F(1, 29) = 6.93; p < .05$). The decade distance effect for incompatible number pairs (75 ms) was smaller than the decade distance effect for compatible pairs of numbers (82 ms; $t(29) = -6.89, p < .05$). A three-way interaction between unit distance, decade distance and compatibility ($F(1, 29) = 5.72, p < .05$) was observed.

Figure 10: Compatibility effect (difference between incompatible and compatible trials) for each SOA depicted separately for small and large unit distances in Experiment 3. SOA was coded negatively when the relevant decade digit appears before the unit.

Taken together, these results imply that the effect of compatibility was modulated by unit distance, decade distance and SOA. Moreover, in line with the prediction of the
interference model (see Dehaene et al., 1993), the influence of the units was stronger for positive SOAs than for negative SOAs, as indicated by the numerically regular (but non-significant) compatibility effects. Note that the compatibility effect works against the decade distance effect. Therefore, finding a null effect does not mean that units did not exert any influence on the magnitude comparison process. It merely means that the influence was not strong enough to overcome the decade distance effect.

Since results from Experiment 1 and the graphic impression of the data in Experiment 3 (see Figure 10) suggest a complex interplay of unit distance, decade distance, and (short and long) SOA with compatibility, we performed an analysis akin to Experiment 1, taking into account only short SOAs (-100 ≤ SOA ≤ 100). Most importantly, there was (i) a significant main effect of compatibility, indicating that incompatible trials were responded to more slowly than compatible trials (655 ms vs. 650 ms, F(1, 29) = 4.62, p < .05), and (ii) a significant interaction of compatibility with SOA (F(2, 58) = 5.96, p < .01) which was due to an increase of the compatibility effect with increasing SOA (-2 ms < 6 ms < 11 ms, as indicated by the significant linear by linear contrast F(1, 29) = 13.55, p < .01).

2 X 2 X 2 ANOVA for Each SOA Separately

To investigate the interaction of the compatibility effect with SOA in more detail, we computed a 2 X 2 X 2 ANOVA comprising the factors compatibility, unit distance and decade distance for each SOA, separately. Table 4 gives an overview of the relevant main effects and interactions. The impression of the analyses using aggregated SOAs is confirmed by this analysis: The units exert the largest influence in SOA conditions +50, +100, and +200 ms. Here, compatibility approaches statistical significance, and can be regarded as being significant when tested using a students t-test, one-tailed. Moreover, in the reference condition (SOA = 0) a significant regular compatibility effect (F(1, 29) = 2.99, p < .05, one-tailed) was observed. Note that in this condition compatibility interacted with unit distance (F(1, 29) = 12.01, p < .01). This interaction was due to the fact that the compatibility effect was larger for large unit distances than for small unit distances (t(29) = 3.47, p < .01).
Table 4: Results of the ANOVAs in Experiment 3 for each SOA separately. Significant F-values (degrees of freedom = (1, 29)) and the respective p-values are bold printed.

<table>
<thead>
<tr>
<th>SOA</th>
<th>Compatibility</th>
<th>Decade distance</th>
<th>Unit distance</th>
<th>Compatibility X decade distance</th>
<th>Compatibility</th>
<th>Unit distance</th>
<th>Compatibility X unit distance</th>
<th>Decade distance</th>
<th>Unit distance</th>
<th>Compatibility X unit distance</th>
</tr>
</thead>
<tbody>
<tr>
<td>-400</td>
<td>F = 5.76, p &lt; .05</td>
<td>F = 93.47, p &lt; .01</td>
<td>F = .37, p = .55</td>
<td>F = .35, p = .56</td>
<td>F = .07, p = .80</td>
<td>F = .78, p = .39</td>
<td>F = 2.83, p = .10</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-200</td>
<td>F = 3.65, p = .07</td>
<td>F = 197.31, p &lt; .01</td>
<td>F = .91, p &lt; .01</td>
<td>F = 4.60, p = .35, p &lt; .05</td>
<td>F = .11, p = .74</td>
<td>F = .30, p = .59</td>
<td>F = 2.81, p = .10</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-100</td>
<td>F = .48, p &lt; .01</td>
<td>F = 228.26, p &lt; .01</td>
<td>F = 2.29, p &lt; .01</td>
<td>F = 1.43, p = .31</td>
<td>F = 4.42, p &lt; .05</td>
<td>F = .11, p = .75</td>
<td>F = 2.81, p = .10</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-50</td>
<td>F = .21, p = .65</td>
<td>F = 262.84, p &lt; .01</td>
<td>F = .27, p &lt; .01</td>
<td>F = .22, p = .60</td>
<td>F = 8.62, p &lt; .01</td>
<td>F = .23, p = .63</td>
<td>F = .10, p = .55</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>F = 2.99, p &lt; .01</td>
<td>F = 450.21, p &lt; .01</td>
<td>F = 1.01, p &lt; .01</td>
<td>F = 1.56, p = .32</td>
<td>F = 12.01, p &lt; .01</td>
<td>F = 1.56, p = .60</td>
<td>F = .45, p = .51</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>50</td>
<td>F = 21.36, p &lt; .01</td>
<td>F = 263.02, p &lt; .01</td>
<td>F = 5.20, p &lt; .01</td>
<td>F = 1.84, p &lt; .01</td>
<td>F = 2.43, p &lt; .01</td>
<td>F = 1.84, p = .19</td>
<td>F = .11, p = .75</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>100</td>
<td>F = 2.02, p = .17</td>
<td>F = 300.73, p &lt; .01</td>
<td>F = 16.98, p &lt; .01</td>
<td>F = 4.90, p &lt; .05</td>
<td>F = 2.37, p &lt; .01</td>
<td>F = 1.13, p &lt; .01</td>
<td>F = .04, p = .85</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>200</td>
<td>F = 2.81, p &lt; .10</td>
<td>F = 284.60, p &lt; .01</td>
<td>F = 4.18, p &lt; .01</td>
<td>F = 2.24, p &lt; .01</td>
<td>F = 4.64, p &lt; .05</td>
<td>F = 1.13, p &lt; .01</td>
<td>F = .36, p = .10</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>400</td>
<td>F = .81, p &lt; .38</td>
<td>F = 328.50, p &lt; .01</td>
<td>F = 1.39, p &lt; .01</td>
<td>F = .38, p &lt; .01</td>
<td>F = 5.05, p &lt; .05</td>
<td>F = .38, p = .15</td>
<td>F = .15, p = .55</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Regression Analysis per SOA

To understand the relative impact of compatibility on the magnitude comparison process in relation to the other experimental factors involved, we have conducted a regression analysis over items. The analysis included overall absolute distance, logarithm of the absolute distance, absolute problem size, logarithmic problem size, logarithmic decade distance, absolute unit distance, logarithmic unit distance, compatibility and signed logarithmic unit distance. Signed logarithmic unit distance was computed by multiplying logarithmic unit distance with -1 for incompatible trials and +1 for compatible trials. Thus, the signed logarithmic unit distance parametrically codes for compatibility. Note that both a distance of -1 and a distance of +1 would enter the analysis with the same value (0). Therefore, we added +1 to all distances before computing the logarithm. Regressions were computed for each SOA separately. Since regression analyses in earlier experiments have shown that (logarithmic) overall distance often becomes the most important predictor and overall distance comprises both decade and unit distance, we decided to make logarithmic decade distance the obligatory first predictor in a step-wise regression analysis. This offers the opportunity for unit-related factors to enter the model as a significant predictor, because its influence is not automatically captured by overall distance.

The signed logarithmic unit distance became a significant predictor in SOAs +50 and +100 ms as well as in the reference condition with simultaneous presentation (SOA = 0). A full overview of the results is provided in Table 5. This corroborates the results from the ANOVAs: When the unit digits appeared first (positive SOAs), their influence on the comparison process was larger as compared to the conditions when the decades appeared first (negative SOAs). This was limited however, to the SOA range 0 to +100 ms. When the units appeared 200 ms or 400 ms prior to the decade digits, no reliable influence on the response process was evident.

When absolute decade distance was included as a predictor, the results were well comparable. However, in the simultaneous condition, decade distance was favoured over signed logarithmic unit distance. Note however, that decade distance is confounded with compatibility. Incompatible trials have a larger decade distance than compatible trials. Moreover, signed logarithmic unit distance still was a significant predictor (p = .04) in that condition but the respective t-value was slightly smaller (-2.068) than the respective value for decade distance (2.136, p = .034). Therefore, compatibility indirectly comes into play even when absolute decade distance is included.
Table 5: Results from a step-wise regression analysis per SOA including corrected amount of explained variance and the significant predictors and their respective beta-values, t-values (degrees of freedom = 239), and p-values.

<table>
<thead>
<tr>
<th>SOA</th>
<th>$R^2_{corrected}$</th>
<th>predictors</th>
<th>$\beta_{standardised}$</th>
<th>t-value</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>-400</td>
<td>.496</td>
<td>Log. decade dist</td>
<td>.190</td>
<td>1.047</td>
<td>.296</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Abs. problem size</td>
<td>-1.321</td>
<td>-3.881</td>
<td>&lt; .001</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Abs. overall dist.</td>
<td>-.888</td>
<td>-4.961</td>
<td>&lt; .001</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Log. problem size</td>
<td>1.016</td>
<td>2.983</td>
<td>.003</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Compatibility</td>
<td>.150</td>
<td>2.597</td>
<td>.010</td>
</tr>
<tr>
<td>-200</td>
<td>.595</td>
<td>Log. decade dist</td>
<td>-.486</td>
<td>-3.768</td>
<td>&lt; .001</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Abs. problem size</td>
<td>-.239</td>
<td>-5.802</td>
<td>&lt; .001</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Abs. overall dist.</td>
<td>-.270</td>
<td>-2.095</td>
<td>.037</td>
</tr>
<tr>
<td>-100</td>
<td>.653</td>
<td>Log. decade dist</td>
<td>-.198</td>
<td>-1.655</td>
<td>.099</td>
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<tr>
<td></td>
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<td>Abs. problem size</td>
<td>-.207</td>
<td>-5.423</td>
<td>&lt; .001</td>
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<tr>
<td></td>
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<td>Abs. overall dist.</td>
<td>-.601</td>
<td>-5.035</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>-50</td>
<td>.672</td>
<td>Log. decade dist</td>
<td>-.011</td>
<td>-.094</td>
<td>.925</td>
</tr>
<tr>
<td></td>
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<td>Abs. overall dist.</td>
<td>-.743</td>
<td>-6.371</td>
<td>&lt; .001</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Log. problem size</td>
<td>-.731</td>
<td>2.659</td>
<td>.008</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Abs. problem size</td>
<td>.652</td>
<td>2.372</td>
<td>.018</td>
</tr>
<tr>
<td>0</td>
<td>.661</td>
<td>Log. decade dist</td>
<td>-.297</td>
<td>-1.741</td>
<td>.083</td>
</tr>
<tr>
<td></td>
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<td>Abs. overall dist.</td>
<td>-.538</td>
<td>-3.423</td>
<td>.001</td>
</tr>
<tr>
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<td>Abs. log. problem size</td>
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<td>-2.244</td>
<td>.026</td>
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<tr>
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<td>Signed log. unit dist.</td>
<td>-.106</td>
<td>-2.068</td>
<td>.040</td>
</tr>
<tr>
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<td>Log. decade dist</td>
<td>-.822</td>
<td>-21.255</td>
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<tr>
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<td>Signed log. unit dist.</td>
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<td>-7.154</td>
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</tr>
<tr>
<td>+100</td>
<td>.623</td>
<td>Log. decade dist</td>
<td>-.887</td>
<td>-18.497</td>
<td>&lt; .001</td>
</tr>
<tr>
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<td>Signed log. unit dist.</td>
<td>-.234</td>
<td>-5.804</td>
<td>&lt; .001</td>
</tr>
<tr>
<td></td>
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<td>Abs. unit dist.</td>
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<td>2.790</td>
<td>.006</td>
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<tr>
<td></td>
<td></td>
<td>Abs. problem size</td>
<td>-1.366</td>
<td>4.613</td>
<td>&lt; .001</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Log. problem size</td>
<td>1.276</td>
<td>4.304</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>+200</td>
<td>.643</td>
<td>Log. decade dist</td>
<td>-.413</td>
<td>-3.416</td>
<td>.001</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Abs. overall dist.</td>
<td>-.394</td>
<td>-3.255</td>
<td>.001</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Log. Problem size</td>
<td>-.081</td>
<td>-2.098</td>
<td>.037</td>
</tr>
<tr>
<td>+400</td>
<td>.481</td>
<td>Log. decade dist</td>
<td>-.206</td>
<td>-1.412</td>
<td>.159</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Abs. overall dist.</td>
<td>-.498</td>
<td>-3.414</td>
<td>.001</td>
</tr>
</tbody>
</table>

Note: Log. = Logarithmic, Abs. = Absolute, Dist. = Distance
To further analyze the complex interplay between the constituting digits in a two-digit magnitude comparison task, an additional regression analysis was computed. The hypothesis was that not only the relevant decade and unit digits are compared to each other, but that also the constituting digits of a given number are compared to each other. The intra-number digit distance describes the numerical distance between decade and unit digit of a given two-digit number, e.g. in 41 the intra-number digit distance is $4 - 1 = 3$. This comparison however is not based on the assigned place-value magnitude of a given digit (i.e. for the digit 3 in 38 the assigned place-value magnitude would be 30) but on the digits’ magnitude (here: 3). There is evidence from an SOA study by Wood and colleagues (2005) for such a digit-by-digit comparison process. Wood and colleagues presented the original stimulus set of Nuerk and coworkers (2001) but manipulated the SOA of the two numbers (Experiment 2). That is, when presenting a number pair like 41_87 the 41 appeared 100 ms in advance of the 87. Wood and colleagues could show that the distance of the constituting digits of the numbers (intra-number digit distance) becomes a reliable predictor if one takes into account the response congruency of this distance. In the above example, the larger number (87) is response compatible in the sense that the decade digit of the larger number is larger than the corresponding unit digit ($8 > 7$). However, the smaller number is response incompatible because the decade digit of the smaller number is larger than the corresponding unit digit.

A regression analysis over items was computed comprising the above mentioned predictors. Additionally, the intra-number digit distance for the smaller (intra dist small), the intra number digit distance of the larger number (intra dist. large) – both coding the response congruency of the respective comparison with the correct decision by the assigned sign -, and the absolute intra number digit distance of larger and smaller number (abs. intra dist. small/large) were included.

The results (see Table 6) clearly support the hypothesis that the digits of each number in a two-digit number comparison task are compared to each other. In conditions SOA = 0 and SOA = 100, these measures even enter regression equation instead of the signed logarithmic unit distance. Thus, these factors seem to explain more variance and thereby are more important for the comparison process. For SOA = 100, in step 2 intra-number digit distance “beats” the signed logarithmic unit distance only by a t-value difference of .928. Both predictors are highly significant at this stage. For SOA = 50 ms condition, signed logarithmic unit distance still enters the regression equation as second most important predictor. Except for SOA = 50 ms, the intra-number digit distance of the smaller number seems to be the more salient feature in the comparison process. The predictor contributes to the comparison process with a positive sign, i.e. the higher the intra-number distance of the smaller number, the more RT increases. Note that the intra-number digit distance of the smaller number is
highly negatively correlated with the signed unit distance \((r = -.688; \ p < .001)\). Therefore, this measure indirectly reflects unit-decade incompatibility.

**Table 6: Results of regression analysis taking into account intra-number digit distances.** (df = 239)

<table>
<thead>
<tr>
<th>SOA</th>
<th>(R^2_{\text{corrected}})</th>
<th>predictors</th>
<th>(\beta_{\text{standardised}})</th>
<th>t-value</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>-400</td>
<td>.494</td>
<td>Log. decade dist.</td>
<td>.236</td>
<td>1.193</td>
<td>.234</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Abs problem size</td>
<td>-1.300</td>
<td>-3.815</td>
<td>&lt; .001</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Abs decade. dist.</td>
<td>-.937</td>
<td>-4.727</td>
<td>&lt; .001</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Log. problem size</td>
<td>.991</td>
<td>2.907</td>
<td>.004</td>
</tr>
<tr>
<td>-200</td>
<td>.632</td>
<td>Log. decade dist.</td>
<td>-.763</td>
<td>15.876</td>
<td>&lt; .001</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Intra dist. Small</td>
<td>.277</td>
<td>6.352</td>
<td>&lt; .001</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Intra dist. Large</td>
<td>-.198</td>
<td>4.538</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>-100</td>
<td>.672</td>
<td>Log. decade dist.</td>
<td>-.296</td>
<td>1.853</td>
<td>.065</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Intra dist. small</td>
<td>.244</td>
<td>5.391</td>
<td>&lt; .001</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Abs dec. dist.</td>
<td>-.588</td>
<td>3.697</td>
<td>&lt; .001</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Abs. problem size</td>
<td>-.113</td>
<td>2.748</td>
<td>.006</td>
</tr>
<tr>
<td>-50</td>
<td>.673</td>
<td>Log. decade dist.</td>
<td>-.077</td>
<td>5.19</td>
<td>.604</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Abs. overall dist.</td>
<td>-.791</td>
<td>5.482</td>
<td>&lt; .001</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Intra dist. small</td>
<td>.167</td>
<td>3.317</td>
<td>&lt; .001</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Compatibility</td>
<td>.114</td>
<td>2.194</td>
<td>.029</td>
</tr>
<tr>
<td>0</td>
<td>.669</td>
<td>Log. decade dist.</td>
<td>-.302</td>
<td>2.216</td>
<td>.028</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Abs. overall dist.</td>
<td>-.569</td>
<td>4.424</td>
<td>&lt; .001</td>
</tr>
<tr>
<td></td>
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<td>Intra dist. small</td>
<td>.165</td>
<td>3.626</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>+50</td>
<td>.672</td>
<td>Log. decade dist.</td>
<td>-.793</td>
<td>20.420</td>
<td>&lt; .001</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Signed log. unit dist.</td>
<td>-.374</td>
<td>7.847</td>
<td>&lt; .001</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Abs. intra dist. large</td>
<td>-.164</td>
<td>3.362</td>
<td>.001</td>
</tr>
<tr>
<td>+100</td>
<td>.608</td>
<td>Log. decade dist.</td>
<td>-.501</td>
<td>3.378</td>
<td>.001</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Intra dist. Small</td>
<td>.225</td>
<td>4.552</td>
<td>&lt; .001</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Log unit dist.</td>
<td>.112</td>
<td>2.776</td>
<td>.006</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Abs. overall dist.</td>
<td>-.338</td>
<td>2.415</td>
<td>.017</td>
</tr>
<tr>
<td>+200</td>
<td>.660</td>
<td>Log. decade dist.</td>
<td>-.519</td>
<td>3.196</td>
<td>.002</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Intra dist. small</td>
<td>.200</td>
<td>4.803</td>
<td>&lt; .001</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Abs. Dec. Dist.</td>
<td>-.367</td>
<td>2.273</td>
<td>.024</td>
</tr>
<tr>
<td>+400</td>
<td>.573</td>
<td>Log. decade dist.</td>
<td>-.200</td>
<td>1.097</td>
<td>.274</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Intra dist. small</td>
<td>.351</td>
<td>6.775</td>
<td>&lt; .001</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Intra dist. large</td>
<td>-.215</td>
<td>4.069</td>
<td>&lt; .001</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Log. size</td>
<td>.161</td>
<td>3.090</td>
<td>.002</td>
</tr>
</tbody>
</table>

Note: Log. = Logarithmic, Abs. = Absolute, Dist. = Distance
2.3.3 Discussion

Experiment 3 revealed several important results: First, by slightly manipulating the way of stimulus presentation we were able to increase the relative importance of the unit digits as compared to Experiment 1. This becomes clear from the interaction of compatibility with unit distance, decade distance, and SOA. Aggregating over several SOA conditions revealed that the most prominent effect of compatibility was present in positive SOAs (i.e. when units appeared first). Moreover, the influence of compatibility was most prominent in short SOAs. These time-course related results are confirmed by the results of the regression analysis. That is, when the unit digits appear after the decades or more than 100 ms in advance of the decade digits, the influence of the unit digits on the comparison process decreases. Participants seem to try to discard the result of the unit digits comparison as soon as the decade digits appear on screen. The appearance of the decade digits resolves the uncertainty concerning the relevance of the digit pair which appeared first. In conditions when the unit digits appeared first, this pair is – theoretically – irrelevant. Participants seem to use this relevance judgement to overrule the results of the unit digit comparison when the units appeared 200 ms or as long as 400 ms in advance of the decade digits. However, the null-effect of compatibility for large unit distances indicates that this was not completely accomplished, very similar to Experiment 1. Remember that we would expect an inverse compatibility in that case due to the larger decade distance in incompatible trials. When unit distance was small, however, the results of the unit digits comparison process could be overruled more effectively.

For large unit distances, we observed a significant compatibility effect in the reference condition (SOA = 0), corroborating the interpretation of Experiment 1. Note that we have used the very same stimulus set as in Experiment 1.

With respect to the SOA modulation of the unit magnitude impact on a two-digit magnitude comparison task, we observed a RT pattern highly consistent with the interference model. That is, the influence of the unit digits was larger for positive SOAs, peaking at SOA = 100 ms. This influence was modulated by unit distance, since it was more prominent for large unit distances. This implies two shortcomings of the study of Dehaene and colleagues (1990): First, the SOA chosen range was too narrow – Dehaene and coworkers limited their SOA variation from -50 to +50 ms – given that the impact of the unit digits peaked at SOA = 100 ms in Experiment 1 and signed logarithmic unit distance became second most important predictor at SOA = 100 ms in Experiment 3. Secondly, the observation that the most prominent effect of unit-decade compatibility was observed for large unit distances points to fact that using a fixed standard and thereby limiting the unit distances to a maximum of 5 minimized the chance of observing relevant unit effects.
Taken together, the results of Experiment 3 are consistent with the results of Experiment 1 and Experiment 2 in that there was an SOA modulation of compatibility. A reliable compatibility effect was observed in the reference condition with simultaneous presentation of units and decades, adding to the strategic interpretation of the null-effect in the respective condition in Experiment 1. Experiments 1 and 3 extend the results of Dehaene and colleagues with respect to the time course of the influence of unit magnitude on two-digit magnitude comparison process. The most prominent effect of unit-digits on the comparison process was observed with SOAs +50 ms and +100 ms. Moreover, the pattern of results in short SOA conditions is totally consistent with the interference model proposed by Dehaene, speaking against a purely holistic representation of two-digit number magnitude.
2.4 General Discussion of Experiments 1 to 3

Study 1 corroborates the idea that the magnitudes of decades and units are processed separately in two-digit magnitude comparison: The unit-decade compatibility effect (Nuerk, Weger et al., 2001, 2004) which is evidence for separate processing of the unit magnitude of two-digit numerals was modulated by SOA in three experiments. The failure to find such a modulation was interpreted by Dehaene and colleagues as evidence for holistic processing of two-digit numbers. However, Dehaene et al. (1990) used a magnitude comparison task with a standard of 55 in which the absolute distance between the two units of the two-digit numbers is restricted to a maximum of 4. In Experiments 1 and 3, we failed to find an SOA modulation of the unit-based compatibility effect for small unit distances, but consistently found SOA modulations of the compatibility effect for large unit distances: If we had used only small unit distances, we would have obtained similar (null) effects as Dehaene and colleagues. Therefore, our results actually confirm their results. However, they also suggest that the interpretation of Dehaene and colleagues does not hold when a set of stimuli with larger unit distances is used.

In sum, the Study 1 suggests that unit-based effects in two-digit number magnitude comparison can be modulated by SOA. This implies that previous null effects are not conclusive. To our knowledge, this is the first study that reports stimulus-induced strategy effects in a simple magnitude comparison task. For the very same stimulus set, we obtained different results depending on (i) whether or not within-decade trials were added to the experiment or (ii) a procedural manipulation jeopardized participants’ strategy of attending only to the left-most digit pair. We elaborate on these strategy effects a bit more in the remainder of the discussion and will focus on two aspects: (i) We will discuss why we found a compatibility main effect in Experiment 2 and Experiment 3 but not in Experiment 1. (ii) We try to give an account for different kinds of compatibility by SOA interactions in the three Experiments.

2.4.1 Strategic Modulation of the Unit-Decade Compatibility Effect

Our data seem to imply that people indeed are able to focus their attention on the decade digits when it is easy and useful. In Experiment 1, it was useful because all trials were between-decade trials. Therefore, it is entirely sufficient to select only the decade digits and to ignore the unit digits if possible. However, if participants successfully do so, we should observe a negative compatibility effect because incompatible trials necessarily have a larger decade distance when overall distance is matched (see introduction for an elaboration). Indeed, this was true for negative SOAs. Thus, observing a null effect for SOA = 0 does not imply that only the decade digits are processed. Rather, it implies that the irrelevant units were inhibited to a greater extent in Experiment 1 than in previous research.
In Experiment 2 between-decade-trials and within-decade trials were equally likely. This means that for half of the trials the magnitude relation of the decade digits was decisive while for the other half of the trials the magnitude relation of the units was decisive. Thus, it is not a particularly useful strategy to only focus on the decade digit in Experiment 2. If our above argument is correct, attention should thus no longer be focused on the decade digits and the compatibility effect should reappear. Indeed, this is what happens in Experiment 2 for the same between-decade stimuli and a very similar experimental setting as in Experiment 1.

In Experiment 3 we have used a procedural manipulation that forced participants to attend to all digits presented – at least initially. That is, by presenting the digits in the centre of the screen – regardless of whether they were decade or unit digits – virtually had the same effect as introducing within-decade trials. The compatibility effect in the reference condition (SOA = 0) reappeared. Numerically, it was still smaller than in Experiment 2. In the small unit distance condition we even failed to replicate the effect. This might imply that participants still focused on the left space from the central fixation sign. However, by introducing the experimental variation of the numbers’ position this strategy yielded valid information only in 5/9 of the trials. Still, when participants know in advance the position of the numbers to appear the compatibility effect is diminished. Note that the positional variation was only as large as half a digits’ horizontal size, i.e. 0.4° visual angle. But even this small positional variation in the majority of the trials was sufficient to significantly increase the unit digits’ impact as compared to Experiment 1. Therefore, the results of Experiment 3 (i) add on the strategic interpretation of the results of Experiment 1 and (ii) corroborate the notion of decomposed processing of units and decades in two-digit magnitude comparison tasks.

This suggests that decomposed processing can be strategically modulated. The compatibility effect depends on whether an attentional focus on one particular location is useful or not. This is important because it implies strategic effects in a magnitude comparison task which was often seen as being highly automatic.

Yet, this does not explain why previous studies have consistently found compatibility effects but Experiment 1 failed to produce them despite using the same stimulus set. Earlier studies have never used a mask which allowed the exact location of the decade digits depending on the mask. In Nuerk, Weger et al. (2001, 2002), a mixed presentation of Arabic numbers and number words has been used. So it did not make as much sense to focus on one particular digit location. In other experiments, we have used diagonal presentation which also alternated randomly between bottom-left / top-right and bottom-right /top-left on the screen (Nuerk, Weger et al., 2004; see also Ratinckx et al., in press). In some experiments (Nuerk, Weger et al., 2004; Wood, Nuerk et al, 2006), the numbers just appeared without
such a type of fixation signs. In sum, in none of our previous experiments a mask helped to
direct spatial attention to select the relevant decade digit.

To conclude, when the experimental settings of mask, their replacement and the
stimulus set allow for a useful attentional focus on the relevant decade digit number, the
compatibility effect can be levelled out. In contrast, when there is no useful a priori attentional
strategy to select the relevant digits (Experiment 2) or the relevant digits’ location is slightly
jittered horizontally (Experiment 3), the compatibility effect is reliably obtained for standard
simultaneous presentation of two-digit numbers.

2.4.2 Strategic Modulation of the SOA Alteration of the Compatibility Effect

In contrast to Dehaene’s results all three experiments produced an SOA modulation of
the unit magnitude effects, namely the unit-decade compatibility effect. However, the results
point to different directions. In Experiment 1 and Experiment 3, the influence of units was
larger when they appeared before the decade digits. In Experiment 2, their influence was
larger when they appeared after the decade digits. The experimental setting was essentially
the same except for the inclusion of within-decade trials in Experiment 2 or a slight change of
the horizontal position of the decade digits in Experiment 3. The divergent results need to be
discussed.

One possible explanation can be derived from the findings of Wood, Mahr and Nuerk
(2005). Wood et al. (2005) used vertical stimulus presentation and manipulated the SOA (i.e.
SOA = -50, 0, 50 ms). However, in contrast to this study, the SOA manipulation was
“diagonal”, i.e., it referred to one unit digit and to one decade digit of the two different two
digit numbers. For instance, for the trial 54_27, the 5 and the 7 would appear together and
the 4 and the 2. While the compatibility effect diminished, regression analyses showed that
another type of second order compatibility became important: the relation of the two digits
appearing together at the same SOA. When the larger/smaller decade digit was also
larger/smaller than the unit digit it appeared together with, responses were fast and
otherwise slow. For instance, in the above example the 5 is the larger decade digit
determining the larger response to the larger number 54, but it is nevertheless smaller than 7
it appeared together with. This second order incompatibility slowed down responses. The
other pair in the above example is second order compatible. The 2 in 27 is the smaller
decade digit and it is also smaller than 4 it appeared together with. Such a second order
compatibility facilitated responses.

It is of particular interest for the present study that the compatibility of the digit pair
which appeared second (i.e., 50ms after the first two digit) explained much more variance
than the number pair which appeared first. In the above example, if the second-order
compatible number pair 4 and 2 appeared second, we would have a faster response than if
the second-order incompatible number pair appeared second. Wood et al. (2005) suggested
that perceptually the second digit pair popped out more than the first one and thereby caught more attention. This might be the reason why the second-order compatibility of the second pair explained more variance.

The pattern of Wood et al.'s results matches exactly that of Experiment 2. The irrelevant unit influenced responses more when it appeared second. It seems that it is harder to suppress under these circumstances. So, as for the existence of the compatibility main effect, the findings of Experiment 2 are again consistent with the results of other studies, while the results of Experiment 1 are not.

The difference between the Wood et al. study and Experiment 2 on the one hand and Experiment 1 on the other hand is again the relevance of the second presentation. In Wood et al., participants had to attend to the digits presented second, because one of these two digits was a decade digit relevant for the magnitude comparison. In Experiment 2, the participants also had to attend to the unit digits because within- and between-decade trials were mixed. EEG studies (Dehaene, 1996) indicate that 50 ms do not suffice to determine whether or not one has to attend to the unit digit. Consequently, participants attended to all digits as revealed by the strong compatibility effect. Only in Experiment 1 participants a priori knew that they would not have to attend to units appearing second. The experimental setting allowed the participants to inhibit whatever appeared after the decades. A similar argument holds for Experiment 3: Here participants knew in advance that all digits appearing right to the pair of digits presented first could well be neglected/inhibited. The inhibition could be initiated before the magnitude relation and the identities of the decade digits were processed. The results seem to suggest that unit digits appearing 50 ms later can indeed be relatively better inhibited when the participants know a priori that they have to inhibit them. Therefore, in Experiment 1 and Experiment 3 the a priori knowledge about the stimulus set and the relevance of the unit digits triggered similar strategies to enhance the overall magnitude comparison by minimizing mental effort. Note that although the unit-decade compatibility effects in Experiment 1 are somewhat stronger when the units appear first, they are still smaller than in the same condition in Experiment 2 in which the unit digits were relevant in 50% of the trials (6ms vs. 34ms).

To summarize, unbeknownst where the relevant digits appear it seems that interference is stronger when the interfering information comes somewhat later. Only with the possibility of selecting relevant information while inhibiting irrelevant aspects the earlier appearance of the relevant information ameliorates performance.

Finally, note that the reversal of the SOA modulation may give an additional explanation for the null effect obtained by Dehaene and colleagues. When the unit digit was relevant in 50% of the trials, we obtained a stronger unit-based effect for decade-first trials. When the unit digit was relevant in 0% of the cases, we obtained a stronger unit-based effect
for unit-first trials. In Dehaene’s study, the proportion of within-decade trials was about 20%, i.e., the relative relevance of the unit was somewhere between our Experiment 1 and Experiment 2 which both revealed SOA modulations of unit effects but in opposite directions. It is also well conceivable that these 20% are just the ratio of unit relevance which produces a null SOA modulation.
3 Study 2:

The Contribution of the Parietal Cortex to Semantic Conflict Resolution – an fMRI Study
3.1 Introduction

This study focused on two main research questions:

1. The first question was whether in the context of a two-digit number magnitude comparison task unit and decade digit magnitude are represented in distinct cortical regions along the hIPS, spatially ordered by numerical magnitude. This would imply a numerotopic organization that would resemble organizational concepts from other domains such as vision, i.e. the retinotopic organization of the occipital cortex. Therefore, this study extends the fMRI study of Wood and coworkers who have used a stimulus set that consisted exclusively of number pairs from different decades. For example, number pairs such as 21_25 were not included in their study. However, in order to disentangle unit and decade digit magnitude information processing and their respective neuronal correlate, one has to include number pairs from the identical decade (henceforth within decade trials).

2. It was investigated which brain structures participate in the resolution of semantic conflicts that emerge from incompatible unit-decade magnitude comparisons in more detail. The numerical characteristics of the stimulus set used here offer the opportunity to take a closer look at semantic interference processing in general. While colour-word tasks or Eriksen tasks only allow a categorical analysis of the conflict, i.e. incongruent versus congruent trials, here we can conduct a more fine-grained, parametric analysis of the fMRI data. The parametric predictor presumably offers a better modelling of the data since data analysis is based on a larger number of data points, with a more precise description of the underlying function. In case there are only two data points, for example, this function is assumed to be linear in nature.

Together, this allows a more precise investigation of the different processes postulated in the model of Nuerk and Willmes (2005), such as the different representations of unit and decade information (1) as well as the integration of all necessary information and the resolution of emerging interferences (2).
3.2 Methods

3.2.1 Participants

12 male right-handed volunteers (mean age = 25.6 years; SD = 6.5, range 19 - 38 years) took part in the study after having given their written consent in accord with the protocol of the local Ethics Committee of the Medical Faculty of the RWTH Aachen University.

3.2.2 Task and Stimuli

Participants had to indicate the position of the larger number from a pair of 2-digit Arabic numbers (see Figure 1) by pressing one of two response keys (right key/above and left key/below).

All stimuli were two-digit numbers in the range of 21–98. Numbers were presented above each other in a central position on the visual display. The same set of 240 stimuli as in Nuerk et al. (2001) was used. In that set of stimuli, overall distance, unit distance and problem size have been matched both absolutely and logarithmically between all stimulus categories (cf. Table 1, pp. B29 in Nuerk et al., 2001). The four digits selected to constitute units and decades of the two two-digit numbers were always different per item in order to avoid confounds related to the visual form of Arabic digits. Additionally, 240 items from the identical decade (within-decade trials) were presented (a subset of 16 items was presented twice) that were matched to the items from different decades with regard to unit distance and problem size (both absolute and logarithmically).

3.2.3 Imaging

For each participant, a high-resolution T1-weighted anatomical scan was acquired with a Philips 1.5 T Gyroscan MRI system (TR = 30 ms, matrix = 256 x 256 mm, 170 slices, voxel size = 0.86 x 0.86 x 2 mm; FOV = 220 mm, TE = 4.6 ms; flip angle = 30°). The anatomical scans were normalized and averaged in SPM2 (http://www.fil.ion.ucl.ac.uk/spm). The average of the normalized anatomies was used for displaying fMRI activation data from the mixed-effects analysis.

Two functional imaging runs sensitive to blood oxygenation level-dependent (BOLD) contrast were recorded for each participant with a Philips 1.5 T Gyroscan MRI system (T2*-weighted echo-planar sequence, TR = 2800 ms; TE = 50 ms; flip angle = 90°; FOV = 220 mm, 64 * 64 matrix; 30 slices, voxel size = 3.4 x 3.4 x 4 mm). In each run, 316 scans were acquired. 5 dummy scans were acquired before each series of 316 scans to allow for steady magnetization. In a rapid event-related design, 576 trials (480 experimental trials + 96 null events) were presented at a rate of 3 s.
3.2.4 Data Analysis

The fMRI time series was corrected for movement and unwarped in SPM2 (http://www.fil.ion.ucl.ac.uk/spm). Images were resampled every 4 mm using sinc interpolation and smoothed with an 8 mm Gaussian kernel. We convolved brain activity over all experimental trials with the canonical hemodynamic response function (HRF) and estimated the effect of parametric regressors representing decade distance and compatibility-based (signed) unit distance on the brain signal for each participant. In order to scale the estimated regression parameters uniformly, the parametric regressors representing decade distance and signed unit distance in between decade trials (see below) and unit distance in within decade trials were standardized to a mean of 0 and a standard deviation of 1. In a mixed-effects second-level analysis, we looked at the cortical regions showing modulation of signal specifically due to decade distance and compatibility-based unit distance in between decade trials (computed as outlined in Figure 1), and unit distance in within decade trials across the sample. Since number magnitude processing is better described by a logarithmically compressed scale (Dehaene et al., 1990), we used logarithmic distances as predictor of brain signal in our analyses. The distances were determined for each pair of two-digit numbers and their values were employed as predictors in the regression analyses of RT and in the parametric analysis of fMRI data. For unit-distance in within decade trials and decade distance in between decade trials we subtracted the smaller number’s value from that of the larger number. Consequently, these predictors were always positive. The signed unit distance in between decade trials, however, was calculated by subtracting the unit value of the smaller number from that of the larger number. Since, the distances were positive when the larger number also had the larger unit digit (e.g. 42_67, because 6 > 4 and 7 > 2, signed unit distance: 7 - 2 = 5) and negative when the smaller number had the larger unit digit (62_37, because 6 > 3 but 2 < 7; signed unit distance: 2 - 7 = - 5; cf. Figure 1), we refer to this predictor as signed unit distance.
3.3 Results

3.3.1 Behavioural Data

ANOVA

RT analysis was based on correct trials only. The trimming procedure excluded RTs outside [200, 1400] ms and - in a second step - trials outside a range of ± 3 SD around a participant’s average RT. We analyzed data by means of a 2 x 2 x 2 repeated measures ANOVA with the factors decade distance, unit distance, and compatibility. A full overview over all mean RT observed in all conditions can be found in Table 7.

*Table 7: Reaction times (standard errors are provided in brackets) for all factorial combinations of the experimentally varied stimulus dimensions (between decade trials: decade distance, unit distance and compatibility; within decade trials: unit distance)*

<table>
<thead>
<tr>
<th>RT (SE)</th>
<th>Compatibility</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Incompatible</td>
</tr>
<tr>
<td>Decade Distance</td>
<td></td>
</tr>
<tr>
<td>Small</td>
<td></td>
</tr>
<tr>
<td>Small</td>
<td>765 (31)</td>
</tr>
<tr>
<td>Large</td>
<td>799 (27)</td>
</tr>
<tr>
<td>Large</td>
<td></td>
</tr>
<tr>
<td>Small</td>
<td>707 (27)</td>
</tr>
<tr>
<td>Large</td>
<td>714 (32)</td>
</tr>
<tr>
<td>Within Decade trials</td>
<td></td>
</tr>
<tr>
<td>Unit distance</td>
<td></td>
</tr>
<tr>
<td>Small</td>
<td>760 (27)</td>
</tr>
<tr>
<td>Large</td>
<td>710 (25)</td>
</tr>
</tbody>
</table>

Note: RT = Reaction Times; SE = Standard Error

In line with results from experiments using similar stimulus sets (e.g. Nuerk et al., 2001; Study 1 of this thesis), there was a main effect of decade distance (F(1, 13) = 44.91, p < .01) which replicates the well established distance effect (cf. Moyer & Landauer, 1967): Larger distances led to 68 ms faster magnitude comparisons. Compatible trials (695 ms) were responded to faster than incompatible (746 ms; F(1, 13) = 111.6, p < .01). In line with results from earlier studies using similar stimulus sets, we observed a significant interaction between unit distance and compatibility (F(1, 13) = 11.76, p < .01). This interaction was due to the fact that for incompatible trials responses were delayed for small unit distances (736 ms) as compared to large unit distances (756 ms; t(13) = 4.17, p < .01; unit distance effect), while no
unit distance effect was present for compatible trials (697 ms vs. 693 ms; t(13) = .5, p = .62). The three-way interaction of all factors was significant (F(1, 13) = 5.42, p < .05). This interaction was due to the fact that the compatibility effect was modulated by unit distance and decade distance: While the compatibility effect was significantly larger for large unit distances when decade distance was small (80 ms vs. 28 ms; t(13) = 3.77, p < .01), no differential influence of the unit distance was observed for large decade distances (47 ms vs. 49 ms for large and small unit distances respectively; t(13) = .12, p = .91).

Trials from one decade were analyzed by means of a t-test for dependant samples: A small unit distance increased RTs by 50 ms (t(13) = 10.01, p < .001; 760 ms vs. 710 ms for small and large unit distances, respectively).

Regression Analysis

In an item-based regression analysis of RT pooled over participants, we examined whether logarithmic unit distance (negative for incompatible trials and positive for compatible trials) and logarithmic decade distance both were reliable predictors of RTs for between decade trials. Though BOLD response and RTs are not directly related with each other, it would be puzzling to find these two predictors to be not predictive for RTs while using them for analyzing fMRI data.

Both logarithmic unit distance (b standardised = -.395, t(237) = -7.27, p < .001) and logarithmic decade distance (b standardised = -.502, t(237) = -9.23, p < .001) were highly predictive for the RT of each item. Overall, these two variables accounted for 33% of the variance (corrected R^2 = .328).

In a similar vein, we analyzed to what degree RTs in within decade trials were a function of the logarithmic unit distance between both numbers: Again, logarithmic unit distance was a significant predictor of the observed RTs (b standardised = -.464, t(222) = -7.81, p < .001) which explained for a total of 21% of the variance (corrected R^2 = .212).

### 3.3.2 fMRI Data

The coefficients describing the effect of decade distance, and signed unit distance for between decade trials, as well as unit distance for within decade trials were estimated in fixed effect models for each participant individually. These data were tested for significance in a random effects model afterwards. Note that, in order to avoid -1 and +1 to enter the signed logarithmic unit distance predictor in between decade trials with 0, we transformed the predictor as follows: First, we added +1 to the absolute unit distance. Then we computed the logarithm, which was multiplied with -1 afterwards in order to code for compatibility. Results for distance related measure(s) and unit-decade compatibility are reported separately:
Numerical Distance or: Are Decade and Unit Digit Magnitude Information Represented in a Numerotopic Way Along the IPS?

To investigate what regions in the brain and especially around the hIPS are activated when numerical magnitude of unit and decade digits have to be processed in a two-digit magnitude comparison task, we contrasted logarithmic decade distance (between decade trials) and logarithmic unit distance (within decade trials) against each other. We contrasted both measures against each other in order to find out whether there is a fine grained differentiation along the IPS in the sense that the numerical magnitude of a given number which is defined by its position in a two-digit number is indicative of which brain region is activated (i.e. numerotopy). Subtracting unit distance in within decade trials from decade distance in between decade trials led to activations in left superior frontal gyrus (BA 8) and right precentral gyrus (BA 6), left inferior frontal gyrus (BA 46), left inferior (BA 20) and middle temporal gyrus (BA 21), left and right precuneus (BA 7), left middle occipital gyrus (BA 18) and right inferior and superior occipital gyrus (BA 18 and BA 19). Additionally, activation in the left hemispheric insula was observed (see Figure 11).
Figure 11: Logarithmic decade distance in between decade trials > logarithmic unit distance in within decade trials (p < .005, uncorrected) masked inclusively with logarithmic decade distance in between decade trials. The lower right part of the Figure shows the bilateral activation in precuneus.

The reverse contrast (unit distance within decade trials > decade distance between decade trials) revealed activations in right middle frontal gyrus (BA 6) and right postcentral gyrus (BA 40). No activation was found in close proximity to the IPS; neither in posterior nor in anterior aspects (see Figure 12). This speaks against a strict concept of numerotopy, i.e. a spatially ordered one-to-one relationship between activated parietal structures and numerical magnitude as defined by a given digit’s position within a two-digit number.
To find out, which aspects of the cortex around the IPS are commonly activated by both distance measures, we chose two different approaches. First, we computed the conjunction analysis for logarithmic decade distance in between decade trials and logarithmic unit distance in within decade trials. Second, we defined both measures as predictors in a multiple regression analysis and only afterwards computed the conjunction of both predictors.

The two predictors used offer independent indices of the relevant numerical distance information that necessarily has to be taken into account when solving the number comparison. Therefore, in the context of the present task, this analysis offers the best to determine, which parietal areas are linked with numerical magnitude processing in general, irrespective of different powers of ten.

The result of the first approach is depicted in Figure 13. We found very circumscribed activity in only three cortical regions: Two clusters of voxels in the left occipital lobe (BA 18) and one in the right occipital lobe (BA 18) showed a significant relation between blood flow and the numerical predictors. Another cluster was located in the left superior parietal lobe.
(BA 7) near the IPS. Table 8 provides the exact Talairach coordinates and Z-values. The conjunction analysis offers a statistical tool to check whether a given region is commonly activated by two or more experimental conditions. Finding a given region to be activated, however, does not necessarily mean that this region is consistently activated by all the conditions invoked (Friston, Penny, & Glaser, 2005). Claiming that the observed region in the left parietal cortex is crucially involved in processing numerical distance in a number comparison task would call for such a consistency check. When looking at the respective activations the two predictors produced, we found this exact region to be activated in both analyses, indicating a high consistency of this activation. This corroborates the interpretation that the observed area around the IPS is intimately linked to the processing of numerical distances and is in line with results from various other studies that linked the IPS with numerical cognition.

Figure 13: Activation in posterior hIPS due to the conjunction analysis (logarithmic decade distance in between decade trials & logarithmic unit distance in within decade trials; p < .005, uncorrected; cluster size > 2).
The results of the second approach are depicted in Figure 14. By and large the results were identical. However, in the first analysis the main activation (as measured by the Z-values) was located in the occipital cortex. In the second approach, the strongest activation was located in the posterior part of the IPS. This region is consistently activated in both analyses and can therefore be regarded as a reliable neural correlate of numerical magnitude processing. Note however, that the parietal activation in the second approach is clearly bilateral. The same holds for the occipital activation which was left lateralized in the first way of analysis and now is present bilaterally.

<table>
<thead>
<tr>
<th>Region (BA)</th>
<th>Number of voxels</th>
<th>Z-value</th>
<th>TC</th>
</tr>
</thead>
<tbody>
<tr>
<td>L Occipital Cortex, Lingual Gyrus (18)</td>
<td>10</td>
<td>3.11</td>
<td>-24</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>-96</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>2</td>
</tr>
<tr>
<td>L Occipital Cortex, Lingual Gyrus (18)</td>
<td>2</td>
<td>2.69</td>
<td>-9</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>-99</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>-3</td>
</tr>
<tr>
<td>R Occipital Cortex, Cuneus (18)</td>
<td>3</td>
<td>2.82</td>
<td>18</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>-99</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>8</td>
</tr>
<tr>
<td>L Superior Parietal Cortex (7)</td>
<td>2</td>
<td>2.80</td>
<td>-27</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>-56</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>50</td>
</tr>
</tbody>
</table>

BA = Brodmann Area; TC = Talairach Coordinates
Figure 14: Results of the multiple regression approach to the common activation for (i) logarithmic decade distance in between decade trials and (ii) logarithmic unit distance in within decade trials ($p < .005$, uncorrected). Note that no lower boundary with regard to the minimal number of voxels in any activated cluster is defined. Therefore even single voxels are depicted when significantly activated.

Semantic Interference

The second central issue in this study was to find out which brain regions are involved in resolving a semantic interference that has its origin in contradicting numerical information during a decomposed processing of unit- and decade digit information in a two-digit magnitude comparison task. To this end, we used the signed logarithmic unit distance in between-decade trials as predictor since it offers a parametric estimate of the semantic conflict induced by diverging unit and decade magnitude comparisons. Activations were observed in left and right middle frontal gyrus (BA 6; for RH: BA 9), and left temporal lobe (BA 37). In both hemispheres, we observed activations along the intraparietal sulcus (see Table 9 and Figure 15). In each hemisphere, two centres of activation were observed: The first is located in the posterior part of the IPS, in close proximity to the activated clusters described above for the conjunction between logarithmic decade distance and unit distance (TC: -30, -57, 47), thus possibly representing magnitude related aspects that are captured.
with the predictor employed (i.e. logarithmic unit distance). The second centre of parietal activation was located in the anterior part of the IPS (TC: -36, -41, 53). It is unique to compatibility related measures, in the sense that we did not observe activity in this region in any of the magnitude related analyses (see above). This site is in good accordance with activations from studies that have focused on either the size-congruity effect (number-Stroop; Pinel et al., 2004) or the ‘classical’ colour Stroop task (van Veen & Carter, 2005).

Figure 15: Signed logarithmic unit distance in between decade trials (p < .005, uncorrected; Cluster size ≥ 10)
Table 9: Local Maxima showing BOLD signal change significantly correlated with logarithmic unit distance in between decade trials, coding parametrically for unit-decade incompatibility (p < .005; uncorrected; cluster size ≥ 10)

<table>
<thead>
<tr>
<th>Region (BA)</th>
<th>Number of voxels</th>
<th>Z-value</th>
<th>TC</th>
<th>x</th>
<th>y</th>
<th>Z</th>
</tr>
</thead>
<tbody>
<tr>
<td>R Middle Frontal Gyrus (9)</td>
<td>41</td>
<td>4.00</td>
<td>51</td>
<td>5</td>
<td>36</td>
<td></td>
</tr>
<tr>
<td>L Superior Parietal Lobe (7)</td>
<td>12</td>
<td>3.26</td>
<td>-27</td>
<td>-61</td>
<td>56</td>
<td></td>
</tr>
<tr>
<td>L Precuneus (19)</td>
<td>83</td>
<td>4.67</td>
<td>-27</td>
<td>-68</td>
<td>31</td>
<td></td>
</tr>
<tr>
<td>L Inferior Parietal Lobe (40)</td>
<td>34</td>
<td>3.55</td>
<td>-36</td>
<td>-41</td>
<td>52</td>
<td></td>
</tr>
<tr>
<td>R Precuneus (7)</td>
<td>34</td>
<td>3.25</td>
<td>18</td>
<td>-53</td>
<td>47</td>
<td></td>
</tr>
<tr>
<td>R Supramarginal Gyrus (40)</td>
<td>14</td>
<td>3.39</td>
<td>39</td>
<td>-48</td>
<td>30</td>
<td></td>
</tr>
<tr>
<td>R Inferior Parietal Lobe (40)</td>
<td>27</td>
<td>3.09</td>
<td>33</td>
<td>-47</td>
<td>41</td>
<td></td>
</tr>
<tr>
<td>L Parahippocampal Gyrus (19)</td>
<td>13</td>
<td>3.35</td>
<td>-21</td>
<td>-50</td>
<td>-8</td>
<td></td>
</tr>
<tr>
<td>L Occipital Cortex, Lingual Gyrus (18)</td>
<td>33</td>
<td>3.93</td>
<td>-30</td>
<td>-70</td>
<td>-4</td>
<td></td>
</tr>
<tr>
<td>L Middle Occipital Gyrus (19)</td>
<td>60</td>
<td>3.71</td>
<td>-36</td>
<td>-86</td>
<td>21</td>
<td></td>
</tr>
<tr>
<td>R Middle Occipital Gyrus (18)</td>
<td>10</td>
<td>2.91</td>
<td>15</td>
<td>-99</td>
<td>16</td>
<td></td>
</tr>
<tr>
<td>R Middle Occipital Gyrus (19)</td>
<td>17</td>
<td>3.97</td>
<td>-42</td>
<td>-87</td>
<td>4</td>
<td></td>
</tr>
</tbody>
</table>

BA = Brodmann Area; TC = Talairach Coordinates

To disentangle the contribution of numerical magnitude (i.e. unit distance) from unit-decade compatibility activation for unit distance in within decade trials was subtracted from unit distance in between decade trials, which also codes for compatibility by its sign. The cerebral areas showing more activity for semantic unit-decade interference than for unit distance were the left middle frontal gyrus (BA 8) and left middle occipital gyrus (BA 19; see Figure 16). Most interestingly however, a cluster of activated voxels emerged in the anterior aspect of the left intraparietal sulcus (BA 40; TC: -36, -38, 52) with a centre of activation only slightly anterior to the left hIPS activation just described above with a reasonable amount of overlap. This corroborates the assumption of two well distinguished areas within the IPS, one activated when numerical magnitude has to be processed and the other, more anterior one linked to the processing of semantic interference. Note that the parietal activation was the most robust in this contrast. Both prefrontal and occipital clusters vanished when the inclusive mask is set to a more conservative level. Thus, these two activations have to be interpreted with some caution due to a possible lack of power.
Figure 16: Activation in the left hIPS in the contrast (signed logarithmic unit distance in between decade trials > logarithmic unit distance in within decade trials; \( p < .005 \), uncorrected) masked inclusively by signed logarithmic unit distance in between decade trials at \( p < .01 \), uncorrected (note that only the parietal activation survived when the mask was chosen more conservatively with \( p < .01 \), uncorrected); Crosshair marks Talairach coordinate \( x = -36, y = -38, z = 52 \).

To find out whether the left-lateralized activation was significantly more active than the respective site in the right hemisphere, flipped the contrast image was flipped and contrasted against the canonical contrast. This allowed for the statistical test of the visual impression of a unilateral activation. Indeed, the left-lateralized activation was active in this contrast (see Figure 17). This indicates a hemispherical specialization in the anterior aspect of the left intraparietal sulcus with respect to the processing of semantic interference in a number processing paradigm.
Figure 17: (Signed logarithmic unit distance in between decade trials > logarithmic unit distance in within decade trials, masked inclusively with signed logarithmic unit distance in between decade trials) > the same contrast flipped around the y-axis (left – right reversed). Crosshair marks Talairach coordinate x = -36, y = -38, z = 52.
3.4 Discussion

This study served two goals: First, it aimed to find out whether there is evidence for a numerotopic organization of the neural correlate of unit and decade digit magnitude representation in the context of a two-digit magnitude comparison task. The second aim of this study was to take a closer look at the role of the IPS in the context of semantic interference processing.

3.4.1 Number Magnitude

As far as the first question is concerned, we did not find convincing evidence for any kind of numerotopic organization of unit and decade digit magnitude along the hIPS. Neither did the decade digits reveal any strong activation along the IPS unique to decade distance, nor did we observe any activation that was unique to unit distance in within decade trials. In contrast, in the conjunction analysis for unit and decade distance we did observe a very circumscribed activation in the posterior, medial bank of the IPS (TC: -27, -60, 51). This region falls superior and slightly posterior to the published coordinates for numerical distance effects in the study of Cohen Kadosh and colleagues (2005; -24, -55, 42), and may correspond to the area vIP, which is thought to be intimately linked to the processing of numerical information (Hubbard et al., 2005). Furthermore, activity in this region was observed in many number processing studies indicating a close link to processing numerical magnitude information (e.g. Eger et al., 2003; Thioux et al., 2005). However, the view that the activations along the intraparietal sulcus are specifically related to the representation of numerical magnitude has recently been challenged in several ways: First, based on literature from different domains of cognitive psychology, Walsh (2003) postulated “A Theory of Magnitude (ATOM; p. 483)”. The central claim is that time, space and quantity are part of a general magnitude system, which is subserved by the parietal cortex. This would indicate that the parietal cortex is involved in the processing of various continuous dimensions, rather than being magnitude specific (see also Knops et al., 2006 for a discussion of stimulus specificity of the parietal cortex). In a similar vein, Fias and colleagues (2003) postulated a neural overlap hypothesis: Based on their findings in an fMRI study these authors propose a common mechanism for the processing of symbolic and non-symbolic magnitude information with a common neural substrate in the left parietal cortex. Interestingly, this area is in close proximity to the focus of activation described above (14 mm; note that the activated cluster in the study of Fias and colleagues contained 207 voxels). Second, Goebel, Johansen-Berg, Behrens and Rushworth (2004) suggested that the parietal cortex is active in most of the above mentioned number processing studies for reasons different from numerical distance: Based on their fMRI results these authors suggest to understand parietal cortex activations as being linked with more general task demands such as the “representation of the different
possible response alternatives that might be selected” (p. 1545). In the present study we cannot disentangle these different functions the hIPS is associated with. However, given the parametric analyses we have conducted it seems rather unlikely that the activation in medial aspects of the hIPS is due to continuously increasing amount of response alternatives with increasing numerical distance between the two numbers presented. It may still be possible that the observed activation is due to an increasing difficulty that is inseparably confounded with numerical distance in a magnitude comparison task. But Barch and colleagues (1997) have demonstrated that increasing task difficulty in the context of a working memory task is associated with activation of the anterior cingulate, the right inferior frontal cortex and the basal ganglia rather than the hIPS. Note that we cannot assume any hemispheric specialization since we observed similar but bilateral activation for unit and decade distance in a multiple regression analysis. However, the centre of activation was in the posterior part of the IPS in both analyses. Therefore, there seems to be a larger involvement of posterior areas in the IPS in numerical distance processing.

### 3.4.2 Semantic Interference

The second question goes beyond the pure scope of the domain of numerical cognition. What role does the parietal cortex play in resolving semantic interference that emerges from incompatible unit-decade magnitude comparisons? To answer this question we analyzed which parts of the brain are activated by changes of the parametrically modelled amount of unit-decade (in-)compatibility. Beyond activation in other brain areas, we observed an activation in the anterior aspect of the left intraparietal sulcus (-36, -41, 52) that seems to be sensitive to the semantic conflict that arises from contradicting stimulus inherent information for several reasons: First, it is spatially distinct (i.e. more anterior and medially located) from the activations linked with numerical distance in this study (see Figure 18). The centres of activation were (-36, -41, 52) for the effect of interference and (-27, -60, 51) for the conjunction analysis of decade distance and unit distance. Therefore, they were more than 19 mm apart. Second, to make sure, the activation was not due to unit distance we contrasted the signed logarithmic unit distance in between decade trials against the logarithmic unit distance in within decade trials (bd_lgd1_incl_comp > wd_lgd1). In doing so, we sought to “partial out” the aspects of unit magnitude processing from the interference aspects of this activation (see Figure 16). The most important result of this contrast was the observation that the activation in the left anterior aspect of the hIPS prevailed, corroborating its independence from numerical distance. Third, this activation is in good accordance with activations observed in cross-dimensional Stroop-like paradigms of Pinel and coworkers. In their study the authors used magnitude and intensity judgments concerning the numerical and physical size, as well as the luminance of the presented stimuli, i.e. Arabic numbers. They found that numerical and physical size judgments both activated the left IPS and, more
importantly for the present study, the cross-dimensional interference was associated with activation of an area in left anterior aspect of the IPS. Fourth, the left parietal activation is not restricted to numerical interference paradigms since other studies employing non-numerical Stroop paradigms also find this region of the brain activated (e.g. Liu, Banich, Jacobson, & Tanabe, 2004).

The exact role of this region remains speculative. Based on their findings in a spatial Stroop paradigm, Liu and coworkers (2004) comprehend this region as interface between dorsolateral prefrontal cortex (DLPFC) and posterior cortex that passes the DLPFC’s modulatory signals. This view is consistent with the observed activation in left prefrontal cortex (BA 8). These two brain regions may form a neural circuit that is particularly involved in resolving the semantic interference. Given that prefrontal areas are usually associated with strategic and executive (control) functions, the left anterior IPS may be responsible for linking numerical and executive aspects of the task. Beyond, it may be involved in the assignment and maintenance of attention to posterior processing streams (see also Corbetta, Kincade, Ollinger, McAvoy, & Shulman, 2000; Giesbrecht, Woldorff, Song, & Mangun, 2003). However, the parietal structures more frequently associated with attention orienting and maintenance are located in posterior, superior parietal cortex (BA 7; see e.g. Dehaene et al., 2003; Thut, Nietzel, & Pascual-Leone, 2005; Corbetta & Shulman, 2002). In sum, we would like to propose that the anterior aspect of the left hIPS is associated with semantic interference rather than reflecting numerical magnitude aspects of information processing.

This becomes even more likely given the fact that brain areas involved in the processing of numerical distance information were spatially distinct from the areas activated by the semantic interference: While numerical distance seemed to activate bilateral posterior parts of the IPS, the interference activation was strictly left-lateralized (see Figure 17). More specifically, the interference activated areas in the medial wall of the anterior left IPS (see Figure 18).
Figure 18: Functional differentiation of the IPS. Superimposed on the mean group anatomy: (signed logarithmic unit distance – logarithmic unit distance in within decade trials masked inclusively by signed logarithmic unit distance at p = .05; cyan) & (conjunction of logarithmic decade distance in between decade trials & logarithmic unit distance in within decade trials; red); all contrasts at p < .005, uncorrected

3.4.3 Hemispheric Specialisation – Left- or Right-Lateralised?

Another aspect of the present data needs to be discussed. Wood, Nuerk and colleagues (2006) used the same task with a different set of stimuli (i.e. there were only trials from the different decades) but observed a right lateralized activation for signed unit distance. However, we observed a left lateralized activation. How can we explain this? This difference in hemispheric dominance might be due to stimulus-set induced attentional differences in the overall strategy that the participants have employed: In the domain of visual perception, a left hemispheric dominance is postulated for the perception of local features, contrasted by a
right hemispheric dominance for global features (e.g. Fink et al., 1997; Navon, 1977). In the context of a two-digit magnitude comparison task, one might argue that unit distance represents a local feature while overall distance and decade distance (constituting the largest part of overall distance) is a global feature. Therefore, including within decade trials into the stimulus set might have altered the processing strategy and attentional focus of the participants as compared to the study of Wood, Nuerk et al. (2006). Instead of focussing on the decade digit (i.e. the overall distance or the global aspects) participants might have engaged a processing strategy that focused stronger on the local features of this comparison process. This might have resulted in a more decomposed magnitude comparison of the corresponding unit and decade digits in both numbers. There is indeed some evidence in favour of an altered overall processing strategy in the behavioural data: First, the main index of decomposed magnitude processing, the compatibility effect is larger in the current study (51 ms) than it was in the study of Wood, Nuerk et al. (2006; 7 ms [sic!]; t(23) = 8.02, p < .001). Second, Wood and colleagues did not observe any interaction between compatibility and unit or decade distance. In the present study distance measures did interact with compatibility. We observed a three way interaction of compatibility, decade distance and unit distance that indicated the differential influence of compatibility depending on these factors. The influence of compatibility was indeed strongest when the unit distance was large, indicating (i) a stronger influence of unit distances on the comparison process as compared to the data of Wood, Nuerk et al, where no such interaction was present, and (ii) that this influence was semantically mediated by the numerical distance between the unit digits. As laid out in the introduction, the hemispheric dominance of those parts of the brain devoted to the processing of unit-decade compatibility remains contradictory: Our results are in line with the results observed by Ratinckx and colleagues (in press) who found the RH to be more engaged in a holistic processing strategy while the LH is associated with a more analytic processing. Since all three studies used different stimulus sets (e.g. with regard to the salience of the unit digits) we want to attribute the observed differences in hemispherical dominance to different stimulus sets that might have resulted in different processing strategies of the participants. This is in line with the results of Study 1. We found the compatibility effect to be modulated by the importance of the unit digits in the stimulus set used. In detail, the compatibility effect was higher when the stimulus set comprised within decade trials, as compared to a stimulus set consisting only of between decade trials.

To sum up, our results indicate a strategic difference between the present study and the study of Wood, Nuerk and colleagues (2006) in that the participants paid more attention to the unit digits which in turn resulted in a more decomposed processing. Analytic processing has been shown to be dominated by the left hemisphere.
3.4.4 Anterior Cingulate Cortex Activation

Another intriguing aspect of the present results merits discussion. Van Veen and Carter (2005) recently discussed the role of the anterior cingulate cortex in the course of interference. They provided evidence in favour of ACC involvement in both response conflict and semantic conflict detection. Although the postulated independence of the two mechanisms is questionable, it is in good accordance with findings from other studies (Van Veen, Holroyd, Cohen, Stenger, & Carter, 2004; Ullsperger & von Cramon, 2001; Fan et al., 2003). However, these results are inconsistent with the results of the present study. We failed to find the ACC active in any conflict related analysis. Since the interference in this study is based on numeric semantics and modulated by other semantic factors (i.e. unit distance, see above), we suggest the compatibility effect to reflect a pure semantic conflict (see Nuerk, Weger et al., 2005 for a similar argument). The absence of any ACC activation casts some doubt on the involvement of the ACC in semantic conflict situations. In contrast, we did observe a left lateralized activation in middle frontal cortex (BA 8) which might be interpreted in terms of inhibition (cf. Fan et al., 2003). Since we did not observe any activation in premotor cortex or supplementary motor areas, we refrain from the view that in case of incompatible trials a wrong manual response was prepared. Thus, the activation in middle frontal gyrus may be interpreted in two different ways: Either it reflects the inhibition of erroneous responses in case of incompatible number pairs or it is associated with the inhibition if the ‘wrong’ digit, i.e. the unit digit which would lead to a different response.

To conclude, Study 2 revealed two relevant aspects about the neural correlates of two-digit number processing.

First, we could demonstrate that the IPS is not organized in a numerotopic way. Neither decade distance nor unit distance activate unique and specific areas in the IPS. In contrast, we could show that areas located in posterior parts of the parietal cortex bilaterally are involved in processing numerical magnitude information.

Second, the semantic interference induced by unit-decade incompatibility activated an area in the left anterior part of the medial wall of the IPS. This area is distinct from the magnitude related brain regions. We suggest that this area is involved in either resolving the semantic conflict between unit and decade digit information or in linking numerical and executive aspects of the task.

Thus, Study 2 contributes to the parcelling of the areas around the IPS more specifically. We could demonstrate that within the IPS at least two cortical networks are active when two-digit number magnitude comparison is executed. One is being located in the medial anterior part of the IPS, the other one in the posterior IPS.
4 Study 3:

On the Functional Role of Human Parietal Cortex in Number Processing:

How Gender Mediates the Impact of a ‘Virtual Lesion’ Induced by rTMS

Published in Neuropsychologia, 44(12):2270 – 2283.
(Co-authored with H.-C. Nuerk, R. Sparing, H. Foltys, and K. Willmes)
4.1 Introduction

Although the hIPS is the core brain region subserving number magnitude representation, it has never been chosen as the specific stimulation site in a TMS study employing 1Hz stimulation to induce a transient ‘virtual lesion’. Therefore, we investigated the effect of a ‘virtual lesion’ of left hIPS on number processing. We have chosen the left hIPS because recent results (Sandrini et al., 2004; Cohen Kadosh et al., 2005) seem to suggest a somewhat more essential role of the left hIPS for number comparison as compared to the homologue area in the right hemisphere. Left hemispheric rTMS over dorso-lateral prefrontal cortex (DLPFC) was also found to modulate the cognitive bias in a random number generation task by Knoch, Brugger, and Regard (2005). PFC has been shown to contain a large number of fibres projecting onto ipsilateral parietal cortex (e.g. Petrides & Pandya, 1984, 1999) which might have mediated this effect.

The area around the hIPS is assumed to encode a magnitude representation bilaterally. Homologous areas in the left and right parietal cortex are known to be transcallosally connected. Such transcallosal connections have been assumed to be stronger for women (e.g. Steinmetz, Staiger, Schlaug, Huang, & Jancke, 1995 but see Luders et al., 2003 for a contradicting view). Accordingly, De Gennaro et al. (2004) observed that the influence of TMS applied to one hemisphere on the performance of the other hemisphere is stronger in female participants as compared to male participants. In a similar vein, Huber, Schneider, and Rollnik (2003) found female patients suffering from schizophrenia to be more susceptible to the effects of rTMS than male patients. Interestingly, this gender specific effect was restricted to performance in a task using numbers (i.e. number-connection task). Since behavioural gender differences in number processing and calculation have been reported (e.g. Benbow & Stanley, 1983; Deloche et al., 1994; Carr & Davis, 2001), we examined the differential gender influence of TMS on number magnitude comparison tasks.

We were interested in two aspects of two-digit number processing.

1. We wanted to investigate whether the left hIPS was involved in two-digit number magnitude processing. Therefore, we examined the distance effect for two-digit numbers with and without rTMS stimulation.

2. Correctly representing the Arabic place-value system is a necessary prerequisite for processing multi-digit Arabic numbers. This encompasses (i) the correct encoding of the different digits and (ii) correctly attributing the respective power of 10 to a particular digit depending upon its position in a multi-digit string. As laid out above the ease of integration of position and digit value information can be indexed by the compatibility effect. Therefore, we examined the compatibility effect for two-digit numbers with and without TMS to study whether the left hIPS is also functional in place-value integration in the Arabic number system.
Since men and women may be differentially susceptible to TMS (Huber et al., 2003), probably reflecting gender differences in transcallosal transfer (cf. De Gennaro et al., 2004), we also examined whether these effects were different in men and women.
4.2 Materials and Methods

4.2.1 Participants

12 neurologically healthy native speakers of German (6 female; mean age 24 years, range 21 – 32); 6 male participants; mean age: 32.7 years (range: 24 – 60) gave their written informed consent for the study. All participants were right-handed according to the Edinburgh Handedness Inventory (mean laterality score +94.1; ranging 62.5 to 100) and had normal or corrected to normal vision. The study was approved by the local Ethics Committee of the Medical Faculty at the RWTH Aachen University. Participants were paid 20 €.

4.2.2 Stimuli and Procedure

Stimulus material comprised 240 different two-digit number pairs between 21 and 98. Half of them consisted of numbers from different decades (between-decade trials, e.g. 47_62), while the other half consisted of numbers from the same decade (within-decade trials, e.g. 21_26). For between-decade trials, decade distance (i.e. for the number pair 42_67 the decade distance is 6 – 4 = 2; 1 – 3: small; 4 – 7: large) and compatibility (number pairs were incompatible when magnitude comparison of decade digit and unit digit would lead to different responses; e.g. for 47_62, 4 < 6 but 7 > 2) were manipulated. Overall distance, decade distance and problem size (i.e. the sum of both numbers\(^5\)) were matched both absolutely and logarithmically between respective stimulus groups (cf. Nuerk et al., 2001). 120 number pairs from the same decade (within-decade trials) were included to prevent participants from directing attention to decade digits only. This attentional bias has been shown to reduce the impact of unit digits on the comparison process (Knops, Nuerk, & Willmes, 2003). Within-decade trials were matched to between-decade trials for unit distance and problem size.

Number pairs were presented above each other on a 20" monitor (100Hz) in grey colour (RGB 222, 222, 222) against a black background using Presentation software (http://nbs.neuro-bs.com/presentation). Stimuli extended to a visual angle of 1.4° vertically, and 2.1° horizontally. The distance between the upper boundary of the lower number and the lower boundary of the upper number was kept constant at 1.4°. A vertical arrangement of the number pairs does not substantially influence the effects of interest (Nuerk, Weger, et al., 2004).

\(^5\) In a magnitude comparison task reaction time is positively correlated with the problem size, i.e. the larger the sum of a given pair of digits the larger the reaction time (e.g. Schwarz & Stein, 1998).
Each participant completed three blocks of 240 trials. Each block was preceded by 15 practice trials. Apart from stimulation of the left hIPS (H), stimulation over the vertex (V) served as control for general effects of TMS. In addition, an individual baseline for the cognitive effects investigated was provided by completing one block with no TMS (N). Temporal order of stimulation sites was balanced such that functional stimulation over the hIPS occurred at all three possible positions across participants (i.e. H-N-V, N-H-V and N-V-H). Experimental conditions were pseudo-randomized for each block and each participant individually.

Each trial started with the presentation of a random dot array extending to 17.2° vertical and 12.8° horizontal angle. We have chosen this mask in order to prevent the mask from being a cue for the exact position of the single digits. Otherwise participants tend to concentrate on the most informative digits (i.e. the decade digits). This reduces the compatibility effect in size and TMS modulations would be harder to detect (cf. Knops et al., 2003; see Experiments 1 to 3 in Study 1). After a 30 ms interstimulus interval, two two-digit numbers appeared on screen until a response key was pressed, but never for more than a maximum of 3000ms. The next trial started after 500 ms in which a blank screen was presented. Figure 19 schematically depicts one trial.

Figure 19: Schematic depiction of one trial: A mask (random dot array) appeared for 500 ms and was replaced by the two-digit number pair after showing a black screen for 30 ms. The stimulus was presented on screen for 3000 ms unless a response button press terminated the trial before.
Participants sat comfortably in a chair with their head fixed via a chin rest resulting in a constant distance of 60 cm from the monitor. Participants were instructed to indicate the position of the numerically larger number pushing the left or right “CTRL” key on a standard keyboard with their left (number in lower position larger) and right (number in upper position larger) index finger. Both accuracy and speed were stressed in the verbal instruction provided by the experimenter. Each experimental block lasted approximately 7 minutes, depending on the overall speed of the participants’ responses. After rTMS blocks (V & H) a 15 minutes pause was included before the start of the next block to “wash out” completely the effects of the prior rTMS stimulation. The whole experiment lasted approximately 60 to 75 minutes.

4.2.3 TMS Parameters

Stimulation sites were defined by means of a frameless, MRI-guided, stereotactical system for coil positioning (http://www.localite.de). For each participant a T1-weighted MRI was obtained (TR 30 ms, TE 4.59 ms, Flip angle 30°, 160 1 mm-slices, no gap) on a 1.5T Philips Gyroscan NT with a standard head coil. The stimulation targets over the vertex and the anterior part of the left hIPS were identified individually and marked by the positioning software (see Figure 20). The TMS-coil was navigated over the stimulation site using the real-time navigation module of Localite software (http://www.localite.de), with the handle pointing backwards, and fastened during stimulation with a customized tripod (see lower right part of Figure 20).

rTMS was delivered at a frequency of 1Hz for 10 minutes immediately before participants completed the task using a Magstim 200 Figure-of-eight coil (Magstim Co., Whitland, UK; 9cm diameter for each wing) attached to a Magstim Super Rapid stimulator. Intensity was set to 60% of the maximum output of the stimulator. This control for intensity was chosen since it has been shown that the motor threshold is unrelated to the excitability of non-motor cortical areas (Stewart, Walsh, & Rothwell, 2001).
4.2.4 Data Analysis

It is important to note that we investigate TMS modulations of specific numerical effects in a within-task approach. General unspecific TMS modulation in a numerical task can have very different specific or unspecific causes. For instance, participants may be faster because they are more alert in TMS conditions or they may be slower in a visual number processing task because visual encoding has been generally affected by TMS. In both cases, one may observe a general TMS effect on RT or errors although numerical representations have not been affected by the TMS manipulation.

Therefore, modulation of numerical effects by hIPS stimulation, irrespective of other more general influences of TMS, are required to be present in order to conclude that the
hIPS is functionally necessary for a specific numerical process. Modulation of the distance effect would offer evidence for the functional necessity of the hIPS for number processing and the mental magnitude representation. In addition, using the compatibility effect as a dependent measure offers the opportunity to examine whether the hIPS is mandatory for integrating unit and decade magnitude information of two-digit numbers.

The trimming procedure chosen excluded RT below 200 ms and outside 3 standard deviations around a participant’s average RT. RT and error rate (ER) were analyzed separately using repeated measures analyses of variance (ANOVA). For computing the ANOVA, ER data were arcsine-transformed (Kirk, 1995) to approximate normally distributed data. Nevertheless, error proportions are reported instead of arcsine-transformed error data to enhance transparency of the descriptive data. ANOVA comprised the within-subject factors decade distance, compatibility, stimulation site, as well as gender as the between-subjects factor. The analysis was based on between-decade trials only since decade distance and compatibility cannot be varied in number pairs from identical decades. If necessary, degrees of freedom were corrected according to the method of Huynh and Feldt (1970). Post-hoc analyses were carried out using t-tests.
4.3 Results

4.3.1 Error Rates

Mean overall error rate was 3.4%. A four-way repeated measures ANOVA for arcsine-transformed error rates was carried out with the factors stimulation site (3 levels), decade distance (2) and compatibility (2) as within-subject factors and gender as between-subject factor. The analysis revealed main effects for decade distance \( F(1, 10) = 36.26; p < .01 \) and compatibility \( F(1, 10) = 27.59; p < .01 \): Participants made more errors in incompatible trials (5.6% vs. 1.2%) or when decade distance was small (5.6% vs. 1.2%). A significant decade distance \( \times \) compatibility interaction was also observed \( F(2, 20) = 16.13; p < .01 \). This interaction was due to the fact that the compatibility effect for small decade distance was significantly larger than for large decade distance \( t(11) = 4.15; p < .01 \). No other main effects or interactions reached significance. In particular, no interaction with stimulation site was observed. Mean error rates are provided in Table 10.

Table 10: Mean reaction times (ms) and error rates (standard errors in parentheses) of the between decade trials under each experimental condition

<table>
<thead>
<tr>
<th>Gender</th>
<th>Compatibility</th>
<th>Decade Distance</th>
<th>No TMS</th>
<th>hIPS TMS</th>
<th>Vertex TMS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>Incompatible</td>
<td>Small</td>
<td>844 (32)</td>
<td>783 (36)</td>
<td>806 (48)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>7.3 (1.8)</td>
<td>9.5 (0.9)</td>
<td>6.7 (2.2)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Large</td>
<td>721 (31)</td>
<td>704 (40)</td>
<td>702 (33)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>3.8 (1.6)</td>
<td>1.5 (0.7)</td>
<td>1.0 (0.6)</td>
</tr>
<tr>
<td></td>
<td>Compatible</td>
<td>Small</td>
<td>762 (39)</td>
<td>742 (48)</td>
<td>746 (55)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>1.7 (1.2)</td>
<td>1.0 (0.6)</td>
<td>1.0 (0.6)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Large</td>
<td>687 (30)</td>
<td>652 (29)</td>
<td>667 (43)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>0.5 (0.5)</td>
<td>0.0 (-)</td>
<td>1.5 (0.7)</td>
</tr>
<tr>
<td>Female</td>
<td>Incompatible</td>
<td>Small</td>
<td>870 (70)</td>
<td>811 (50)</td>
<td>766 (55)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>11.8 (4.3)</td>
<td>9.0 (3.4)</td>
<td>12.8 (3.4)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Large</td>
<td>772 (66)</td>
<td>680 (30)</td>
<td>664 (33)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>1.7 (1.2)</td>
<td>1.0 (0.6)</td>
<td>1.0 (0.6)</td>
</tr>
<tr>
<td></td>
<td>Compatible</td>
<td>Small</td>
<td>810 (66)</td>
<td>696 (29)</td>
<td>698 (33)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>2.2 (1.1)</td>
<td>2.2 (1.1)</td>
<td>1.5 (0.7)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Large</td>
<td>724 (55)</td>
<td>621 (24)</td>
<td>599 (24)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>1.0 (0.6)</td>
<td>1.0 (0.6)</td>
<td>0.5 (0.5)</td>
</tr>
</tbody>
</table>
4.3.2 Reaction Times

A four-way repeated measures ANOVA comprising the same factors as for errors revealed main effects of stimulation site \((F(2, 20) = 5.35; \ p < .05; \ \text{Huynh-Feldt correction factor } \epsilon = .76)\), compatibility \((F(1, 10) = 48.82; \ p < .01)\), and decade distance \((F(1, 10) = 93.24; \ p < .01)\). RT was faster when stimulation was over the vertex, as compared to blocks without preceding stimulation \((t(11) = -2.42; \ p < .05)\). RT differences between other stimulation sites did not reach significance. Participants responded faster on compatible trials than on incompatible ones \((700 \ ms \ vs. \ 760 \ ms)\). A large decade distance evoked faster RT than small decade distance \((683 \ ms \ vs. \ 778 \ ms)\). The four-way interaction \((F(2, 20) = 3.18; \ p.06)\) failed to reach a conventional level of significance \((\alpha = .05)\). Mean reaction times and standard errors are provided in Table 10.

Since we were interested in the specific influence of TMS on the distance and the compatibility effect, we directly analyzed TMS modulation of these respective effects by subtracting RTs for compatible from incompatible trials (compatibility effect), and large decade distance trials from those with small decade distance (distance effect) for each man and woman in the sample. These differences constituted the base for evaluating the net compatibility effect and net distance effect of TMS over vertex and hIPS on cognitive functions by subtracting the control condition \((N)\) from the TMS conditions (see Figure 21 and Figure 22 for net compatibility and distance effects, respectively). If there is a functional link between the distance/compatibility effect and the hIPS, there should be no significant change after vertex stimulation as opposed to hIPS stimulation.
STUDY 3 – RESULTS

Figure 21: Mean net compatibility effect (compatibility effect_{TMS} – compatibility effect_{noTMS}) and standard error for male and female participants for small and large decade distances after stimulation over vertex (light grey) or hIPS (dark grey), respectively.

Figure 22: Mean net distance effect (distance effect_{TMS} – distance effect_{noTMS}) and standard error for male and female participants for incompatible and compatible number pairs after stimulation over vertex (light grey) or hIPS (dark grey), respectively.
Compatibility Effect

Since the compatibility effect is modulated by decade distance (i.e., it is larger for small, more difficult decade distances; Nuerk et al., 2001; Nuerk, Kaufmann, et al., 2004), the impact of rTMS on the compatibility effect was analyzed separately for small and large decade distances. For large decade distances a repeated measures ANOVA comprising the factors site of stimulation (within subject) and gender (between subjects) revealed no significant main effects and no interaction. An analogous ANOVA for small decade distances revealed no main effect of site of stimulation either. However, we observed a significant interaction between gender and site of stimulation (F(1, 10) = 5.93; p < .05), indicating different effects of TMS depending on gender: For female participants the compatibility effect increased due to the TMS stimulation over the hIPS by 55 ms (t(5) = 3.89; p < .05) while no coherent change was observed for men (-42 ms; t(5) = -1.12; p = .32). The reported increase of the compatibility effect was present in all female participants but only in four out of six male participants. A t-test for independent samples revealed that the net compatibility effect after hIPS stimulation was larger for women than for men (55 ms vs. -42 ms; t(10) = 2.43; p < .05).

The TMS modulation of the compatibility effect is particularly remarkable, since we could demonstrate a specific impact of TMS on the numerical effects investigated irrespective of overall RT changes due to general effects of TMS on participants’ alertness (e.g. Campana, Cowey, & Walsh, 2004).

To examine the functional relevance of this TMS modulation, we concentrated on the data for small decade distances (because the compatibility effect was particularly large there) and for women (because the TMS modulation was more consistent for them). For these data, we separated the first half of each block from the second half for each participant and compared the compatibility effect in the first half of the experimental block following TMS to the hIPS (H) to the first half of the block without preceding TMS (N). The rationale behind this procedure is that the effect of a virtual lesion should decrease with increasing temporal distance from stimulation (e.g. Hilgetag, Theoret, & Pascual-Leone, 2001; Mottaghyy, Gangitano, Sparing, Krause, & Pascual-Leone, 2002; Gorsler, Baumer, Weiler, Munchau, & Liepert, 2003). Increase of the compatibility effect due to TMS should be higher therefore in the first half of the experimental block (when the TMS influence is still strong) than in the second half.

Indeed, the effect of hIPS TMS stimulation is stronger in the first half (109 ms; t(5) = 2.82; p < .05) than in the second half (4 ms; t(5) = 0.11; p = .92; see Fig. 5; effect size estimate d = 1.64 vs. d = .66, respectively; Kirk, 1995). Comparing the net compatibility effect of the first half (109 ms) against the net compatibility effect of the second half (4 ms), the effect tended to be numerically larger in the first half (p = .099, one-tailed). The change of the
net compatibility effect in female and male participants due to TMS over the hIPS is shown in Figure 23 for each half of the experimental blocks, separately. Thus, data suggest that the virtual lesion induced by stimulating the hIPS seems to have ceased by the second half of the experimental blocks.

![Graph showing modulation of net compatibility effects](image)

**Figure 23: Modulation of net compatibility effects ((compatibility effect first/second half TMS hIPS) – (compatibility effect first/second half no TMS)) for male (dark grey) and female (light grey) participants in the first (left) and the second (right) half of experimental blocks.**

In sum, for trials with large decade distances, stimulating the hIPS did not significantly influence performance of either male or female participants. For small decade distances, we found a clear impact of rTMS over the hIPS that was gender specific: Female participants showed a specific modulation of the compatibility effect after hIPS stimulation. Moreover, this effect was clearly limited in time. This is in line with previous research suggesting that the effect of a virtual lesion is transient (Hilgetag et al., 2001; Mottaghy et al., 2002; Gorsler et al., 2003).

**Distance Effect**

We analyzed compatible and incompatible trials separately: Since incompatible trials have a larger mean decade distance (with equal overall distance; cf. Nuerk, Weger et al.,...
modulations of distance effects are more likely to occur in incompatible than in compatible trials. Repeated measures ANOVA for compatible trials with site of stimulation and compatibility as within and gender as between subject factors revealed no significant main effects or interactions. An analogous ANOVA for incompatible trials revealed no main effect for site of stimulation. There was a significant interaction between gender and site of stimulation \((F(2, 20) = 4.28; p < .05)\). As for the compatibility effect, this interaction indicates that rTMS differentially affected numerical effects for women and men although compatibility and decade distance were varied orthogonally by and large in the design. Net distance effects for (in)compatible trials and (fe)male participants are displayed separately in Figure 22. Post-hoc analyses showed that for male participants the net distance effect decreased after rTMS over the hIPS by 45 ms \((t(5) = -2.84; p < .05, \text{two-tailed})\). In contrast, we observed an increase of the net distance effect for female participants after rTMS over the hIPS by 34 ms \((t(5) = 2.65; p < 05, \text{two-tailed})\).

Given the temporal variability of the TMS impact on the compatibility effect we separately analyzed distance effects for the first and the second half of the experimental blocks: For male participants, the net distance effect for incompatible trials was decreased by rTMS stimulation over the hIPS \((-70 \text{ ms}; t(5) = -2.74; p < .05)\) in the first half of experimental blocks. In the second half of the experimental block the net decade distance effect was not significantly different from zero \((-23 \text{ ms}; t(5) = -.63; p = .56)\). A t-test for matched samples revealed no differences between both halves of the experimental blocks \((t(5) = -.85; p = .43)\). Female participants showed a numerical increase of the net decade distance effect in the first half of the experimental blocks which failed to reach conventional significance level, however \((\text{difference}: 41 \text{ ms}; t(5) = 1.57, p = .089, \text{one-tailed})\). In the second half of the experiment no significant increase of the net decade distance effect for incompatible trials after application of rTMS over the hIPS compared to control condition without stimulation was observed \((28 \text{ ms}; t(5) = 1.13, p = .31, \text{two-tailed})\). No significant change between both halves was observed \((t(5) = .28, p = .79)\).

To sum up, for female participants inducing a virtual lesion marginally influenced a magnitude related cognitive effect: The decade distance effect for incompatible trials was enlarged after rTMS to the hIPS. These results have to be taken into account with caution, since the observed effects are rather small. For male participants the impact of rTMS was reversed. Here, the decade distance effect decreased after hIPS stimulation. Neither for female nor for male participants these effects significantly covaried with the time elapsed between stimulation and task performance.
4.4 Discussion

The mastery of multi-digit numbers, which is a fundamental skill in everyday-life, requires a comprehensive understanding of the Arabic place-value system. Nevertheless, an increasing amount of research has been devoted to understanding the processing of one-digit numbers and their neural correlates. Little attention has been paid to the processes and brain structures involved in multi-digit processing. In Study 2 we could show the differential involvement of parietal structures in processing numerical magnitude information of two-digit numbers and semantic incongruencies based on contradicting unit-decade magnitude information. While the processing of numerical magnitude seemed to be based on bilateral neural structures, the incompatibility of unit and decade magnitude activates the left hIPS to a stronger degree.

The present study was conducted to investigate the functional relevance of the hIPS for the processes of (i) representing numerical magnitude and (ii) integrating unit-decade information. Recent evidence suggests differences in susceptibility of male and female participants to rTMS (Huber et al., 2003; De Gennaro et al., 2004) probably reflecting gender differences in transcallosal transfer and gender differences in number processing and calculation (e.g. Benbow & Stanley, 1983; Deloche et al., 1994; Carr & Davis, 2001). Therefore, we examined (iii) the role of gender in a two-digit magnitude comparison task by comparing the performance of female and male participants.

The discussion will be organized along the cognitive effects under investigation. First, we discuss the impact of TMS over the left hIPS on the distance effect and the compatibility effect. Since the influence of gender on the task cannot be separated from the cognitive effects we investigated, it will be discussed in the course of the discussion of the respective effects. We conclude this section with a discussion of more general (i.e. anatomical and morphometric) differences between male and female participants and its possible implications for future studies.

First we discuss the observed modulation of the distance effect as a result of stimulation over the hIPS.

4.4.1 Distance Effect

Dehaene et al. (2003) suggest that three parietal circuits are involved in number processing. The hIPS is proposed to be the locus of “a nonverbal representation of numerical quantity, perhaps analogous to a spatial map or ‘number line’ ” (p. 489). Study 2 lends support to this assumption. We observed a network of areas in the bilateral hIPS that was parametrically engaged in processing numerical magnitude of units and decades. Thus, it
seems to be functionally linked to the semantic representation of numbers. If this is true, inducing a virtual lesion in this area should affect processing of the numerical magnitude of the numbers presented. The distance effect serves as a direct measure of processing numerical magnitude information of two given numbers. Thus, if the hIPS is functionally relevant for processing numerical magnitude the distance effect should be affected by inducing a virtual lesion in this brain area. Indeed, the distance effect was modulated.

Gender Moderated TMS Modulation of the Distance Effect

This modulation of the distance effect, however, was observed in an interaction with gender: In female participants, the distance effect marginally increased after rTMS over the left hIPS; in contrast, for male participants the decade distance effect decreased. It is important to note that this study is among the first to demonstrate a differential influence of TMS on the distance effect itself and not just general overall RT effects. In previous research (e.g., Sandrini et al., 2004), often only main effects of TMS were observed. The magnitude comparison task was generally slower after left-hemispheric TMS stimulation. Main effects of TMS on a given task can have task-specific and task-unspecific causes. For instance, participants may produce more errors with TMS in many tasks because the aversive sensation of the electromagnetic impulse interferes with accuracy in the cognitive task at hand. In this example, the TMS effects in a magnitude comparison task would be task-unspecific. Thus they would not imply much about numerical representations in particular. The demonstration of a within-task modulation of the major index of number magnitude representation, namely the distance effect, is therefore important for underlining the functional necessity of the hIPS for this magnitude representation, because it cannot be attributed to general unspecific TMS effects on the task at hand.

Gender Differences in TMS Studies

To account for gender differences in our TMS study with regard to the distance effect, gender differences in other TMS studies will be discussed first. Recently, gender differences with regard to susceptibility to rTMS have been reported in other domains than numerical cognition (De Gennaro et al., 2004; Huber et al., 2003). In these studies the impact of TMS was stronger in female participants than in male participants. De Gennaro et al. (2004) argue that one possible explanation for the observed gender differences is that the corpus callosum (CC) in women is larger than in men (e.g. Steinmetz et al., 1995 but see Luders et al, 2003 for an opposing view). Functional lateralization has been shown to be negatively correlated with callosal size (Hines, Chiu, McAdams, Bentler, & Lipcamon, 1992). Strens et al. (2002) have shown that even subthreshold TMS can lead to significant modulation of cellular activity, as measured by interhemispheric coherence between motor areas. For the motor cortex, an interhemispheric effect of rTMS on the excitability of the contralateral, unstimulated
hemisphere has been reported (Gorsler et al., 2003). Thus, the effect of TMS can extend to homologous areas in the other hemisphere. Taken together, one could suppose that in female participants the contralateral hIPS may be more strongly affected by the left hemispheric TMS, e.g. via transcallosal transfer of the TMS signal. In male participants the smaller degree of transcallosal connection may mitigate the contralateral effects of the TMS. How do these findings and considerations correspond to the gender differences observed for the numerical distance effect?

TMS Modulation of the Distance Effect in Women

Modulation of the distance effect was found in women and men. However, the direction of the modulation differed depending on the participants’ gender. For female participants, the distance effect increased and the account is fairly straightforward: rTMS in the left parietal lobe impairs magnitude representation in areas around the left IPS. Via transcallosal connections, the magnitude representation in areas around the right IPS may also be affected. Magnitude is assumed to be represented on a mental number line for which similar magnitudes are represented in close spatial proximity while magnitudes that are more distant lie farther apart. If access to the magnitude representation on the mental number line is disturbed, the representations may become noisier, because for instance, variability of the magnitude activation of a given number increases (cf. Dehaene, 2001). Such an increase in variability should affect in particular magnitude representations which lie close together (i.e. with small distances) because their representations overlap to a larger extent than representations which are farther apart. Therefore, magnitude comparisons with small distances should be particularly impaired by a virtual lesion in the underlying neural substrate. In contrast, larger distances should be affected to a lesser extent because their representations are so far apart that the additional variability induced by TMS does not really change the comparison process. Consequently, in the TMS condition, magnitude comparisons with small distances take particularly longer, thus leading to an enhanced distance effect. This is exactly what was observed in female participants.

TMS Modulation of the Distance Effect in Men: A Hemispheric Specialization Account

So, why did the distance diminish effect after a virtual lesion in male participants? For a possible account of this finding, a closer look at the data is necessary. In male participants, the distance effect does not generally decrease. It only decreases for incompatible trials while it is unchanged in compatible trials (numerically it even increases slightly). So clearly, the compatibility attribute has to be considered when this decrease is accounted for.

Nuerk et al. (2001, see also Nuerk & Willmes, 2005) have observed that two-digit magnitude comparison cannot be solely based on a single holistic representation. Therefore, they suggested a hybrid model in which three magnitude representations have been
assumed to underlie two-digit magnitude comparison: (i) the holistic magnitude representation previously postulated; and in addition the decomposed representations of (ii) decade magnitude and (iii) unit magnitude. This proposed distinction between holistic (or analogue) and decomposed processing is similar to distinctions made in the field of object perception and representation. In this field, it has long been postulated that the holistic overall configuration or Gestalt of an object is processed to a greater extent by the right hemisphere while the individual features or details of an object are processed to a greater extent by the left hemisphere (for an overview see e.g., Banich, 2004). In a similar vein, one may assume that the holistic representation of magnitude is processed to a greater extent by the right hemisphere while the decomposed representations may be processed to a greater extent by the left hemisphere.

If this assumption is true, the decreased distance effect in male participants after rTMS can be accounted for as follows: Stimulating the left hIPS would then mainly affect the decomposed representations. Since male participants may exhibit less transcallosal transfer (as compared to the female participants), the right hIPS is affected to a lesser extent than the left hIPS. If the right hIPS processes two-digit magnitudes more holistically than the left hIPS (which is impaired), then the task may be solved to a greater extent by holistic processing. Decomposed processing has repeatedly been found to be particularly difficult when the magnitude comparison is incompatible and when the distance between the two numbers is small (Nuerk, Weger et al., 2001, 2002; Nuerk & Willmes, 2005). In these conditions, decomposed processing produces much interference. In contrast, holistic processing does not produce any such interference in incompatible trials. If male participants process two-digit numbers to a greater extent by holistic processing, they should benefit (relatively) most in exactly those conditions in which decomposed processing is detrimental. Such a condition is the small-decade distance /incompatibility condition. In that specific condition, holistic processing should lead to greater improvement than in any other condition (in particular compared to any large decade distance condition). In this way, holistic processing would decrease the distance effect, however, only for incompatible trials for which decomposed processing is detrimental. This is exactly what has been observed in the data: rTMS in males led to particularly faster response latencies in incompatible trials with small decade distances.

Female participants may not show such a specific effect because they may have more transcallosal transfer (e.g. Steinmetz et al., 1995) leading to a globally larger impairment in two-digit number processing. This global impairment can then no longer be overcome by a slight change in processing style (holistic vs. decomposed). Finally, it should be noted that this explanation needs to assume relative differences in processing styles. Even with TMS a compatibility effect prevails in male participants, demonstrating that (albeit reduced) decomposed processing still takes place in addition to holistic processing.
The results are in good accordance with recent behavioural findings of a differential involvement of both hemispheres in number processing. As laid out above, Ratinckx and colleagues (Ratinckx et al., in press) observed a reduced compatibility effect after initial right hemispheric stimulus presentation in a visual half field experiment. This is interpreted in terms of a more holistic processing style of the RH as compared to a more decomposed processing style in the LH.

In addition, in a recent TMS study by Andres and coworkers (2005), a similar differentiation has also been proposed. Based on the interaction of the site of stimulation with the numerical distance of the stimuli in a number processing task the authors suggest that the LH is capable of precise numerical judgements while the RH is restricted to approximate judgements of numerical magnitude. This left-hemispheric specialization is hypothesized to result from a link between (finger) counting strategies and language functions, which are thought to be left-lateralized. Note that in the study of Andres and coworkers, TMS over the left PC had the strongest differential impact on the numerical judgements: After left-hemispheric stimulation the RTs of trials with a small numerical distance were slowed down when compared to RH or sham stimulation. This led to an increased distance effect. When computing the respective estimated effect sizes (Kirk, 1995) from the reported data, the distance effect after LH stimulation (d = .50) was larger than after stimulation of the RH (d = .32), both hemispheres (d = .26) or sham stimulation (d = .27). In contrast, bilateral stimulation affected both small and large numerical distances. This did not increase the distance effect but hampered both hemispheres alike. This TMS finding is also in line with results from patient studies. Damage to the left parietal cortex has frequently been reported to result in severe impairments of numerical abilities such as calculation (Mayer et al., 2003), magnitude approximation (Lemer, Dehaene, Spelke, & Cohen, 2003) or transcoding of two-digit numbers (Blanken, Dorn, & Sinn, 1997; Proios, Weniger, & Willmes, 2002).

To sum up, these results imply a functional role of the hIPS for comparing the numerical magnitude of two numbers with each other. Thus, hIPS activation observed in Study 2 is no mere co-activation without functional significance. The observed results show an interaction with gender. Assuming that female participants exhibit a more pronounced amount of transcortical transfer, a relative specialization of the two hemispheres is consistent with the results of Study 3: While the LH is associated with decomposed processing of two-digit numbers, the RH may rely more on the overall magnitude of two-digit numbers.

### 4.4.2 Compatibility Effect

Comparing two two-digit numbers with each other is not a process as simple as it appears to be at first glance: Beyond correctly representing the numerical magnitude of the units and decades these representations need to be integrated in order to understand the
overall magnitude of the number. The compatibility effect marks the process of integrating the relative numerical value of digits constituting two-digit numbers in accordance with their position. This process presumably relies on parietal cortex since this brain region has been shown to be associated with the spatial, numerical and attentional processes required. If this integration is disturbed, the exact assignment of a numerical value to a digit according to its position in the multi-digit number becomes error prone. If decade magnitude and unit magnitude cannot be distinguished well, unit digit magnitude comparisons should produce stronger interference when they lead to a different result than the decade digit magnitude comparison, i.e. to a larger compatibility effect. Inducing a virtual lesion in the hIPS should thereby lead to an increase of the compatibility effect. Indeed, the pattern of results for a substantial proportion of our sample is consistent with this. In contrast, stimulation over the vertex exerted no significant impact on the compatibility effect. This speaks against a global, non-specific impact of TMS. Thus, the hIPS seems functionally necessary for integrating decade- and unit-digits of two-digit numbers in the course of information processing. That is, the area around the hIPS seems to involved in assigning the respective numerical meaning to a digit according to the position within a given number and building an integrated two-digit number representation. In line with this observation, Schwarz and Heinze (1998) report ERP results from a physical/numerical magnitude comparison task with numbers in different font sizes (size congruity effect) implying that “[…] both, size and numerical information are converted into an integrated representation and potentially interact with each other” (p. 1168). Both dimensional comparisons (physical size and numerical magnitude) lead to amplitude changes over parietal electrodes that vary with distance (i.e. larger distances lead to larger amplitudes). Using fMRI, Pinel et al. (2004) could show the involvement of parietal cortex in resolving size-congruity effects emerging from a conflict between different stimulus dimensions (numerical vs. spatial). Activity in left parietal cortex was increased when cross-dimensional interference occurred (e.g. 2 9: Which number is numerically larger?). According to the authors “number and size appear to converge at an abstract representational level toward a partially overlapping representation in parietal cortex. Indeed, the finding of significant number/size interference in both behaviour and fMRI provides positive evidence that the internal representations of number and size are not merely juxtaposed but share common neural resources” (p. 990). Thus, the parietal cortex seems to be crucial for integrating different streams of magnitude information. In this way, these findings fit with the suggestion that the hIPS is involved in integrating unit and decade digit information for the required comparison.

Another possibility that can account for the present modulation of the compatibility effect is the disruption of a second, more general function of the parietal cortex: As laid out above, the hIPS is involved in the processing of object-based information in the course of
spatial judgments. The integration of unit-and decade digit information encompasses correctly attributing the power of 10 to a particular digit depending upon its position in a multi-digit string. This requires the correct assignment of object-based location attributes to each of the constituting digits. Therefore, it might be possible that the more generic parietal function of providing object-based information has been disturbed by rTMS which resulted in the observed increase of the compatibility effect. However, if this was true, one would not expect this process to interact with a purely semantic dimension of the stimuli, i.e. their decade distance. However, the compatibility effect did only increase after hIPS stimulation for trials with a small decade distance, implying the impairment of the semantic integration of unit- and decade magnitude information. Thus, an impairment of a more general parietal function alone does not seem to provide a suitable account for the present data.

Another intriguing result of the current study is the time-dependent modulation of the compatibility effect for small decade distances, i.e. the impact of the virtual lesion induced by rTMS decreased over time. This modulation was present (in female participants) in the first half of the experimental block, but no longer in the second half (see Figure 23). This is in line with the notion that the impact of offline rTMS at low frequencies is transient, lasting approximately half of the stimulation time (Mottaghy et al., 2002; Robertson et al. 2003). In this study the rTMS train lasted approximately 10 minutes, while one experimental block lasted approximately 7 minutes. Therefore, the results suggest that the impact of a 10 minutes train of 1 Hz rTMS over the parietal cortex lasts at least for approximately 3.5 minutes, leading to a TMS modulation in the first half of the experimental block, but not in the second. This makes sense, whereas the opposite result would be hard to reconcile with previous TMS results. In this way, this finding is a supplementary piece of evidence supporting the validity of the present results. This information about the short persistence of a TMS effect might be useful for planning future rTMS studies employing an offline stimulation design.

To sum up, an increased compatibility effect following rTMS over the hIPS is in line with the assumption of an impaired process of unit-decade digit integration. Moreover, since this modulation was absent after stimulation over the vertex this process appears to be linked to the hIPS. This study is among the first to show a possible functional locus of this process, upon which the place-value system of Arabic numbers is based.

4.4.3 Gender Specific Susceptibility to rTMS

In the following it will be discussed whether the results reflect more general gender differences, which are unrelated to the semantic dimension of two-digit number comparison. That is, can (i) anatomical differences (e.g. differing physical distance between TMS coil and target region (hIPS)) or (ii) mere anatomical size of the stimulated areas produce the observed pattern of results?
At least two possible alternative explanations can be offered to account for the observed differences between male and female participants.

First, anatomical differences might mediate the impact of TMS on the hIPS: The distance between scalp and horizontal aspects of the hIPS is larger for male participants, which might mitigate the impact of TMS on the hIPS per se (see also McConnell et al., 2001). This assumption was tested by measuring in both groups the head circumference, which is highly correlated with distance between TMS entry and target. Male participants had significantly larger head circumference ($t(10) = 4.02; p < .01$). Thus, the impact of TMS may have been diminished for male participants for purely anatomical reasons. However, it does not account for the pattern of results observed here: For male participants the compatibility and the decade distance effects have not only been mediated by rTMS over the hIPS to a smaller degree but also – at least in part – reversed into the opposite direction. In detail, stimulating the hIPS does not significantly influence (albeit numerically reduce) the interference between unit and decade digits in male participants (compatibility effect) whereas it enlarged the compatibility effect for female participants. For the decade distance effect the impact of rTMS over the hIPS was reversed for male as compared to female participants. Neither did head circumference/size perfectly separate female from male participants in the present sample nor did the differential impact of rTMS over hIPS concerning the cognitive effects under scrutiny. That is, two out of six male participants did show an increased compatibility effect after stimulation of the hIPS. While for one male participant the compatibility effect increased from -33 ms to 17 ms after hIPS TMS, the other one revealed a RT pattern (17 ms to 68 ms) very similar to that exhibited by female participants, including time-dependent modulation of the compatibility effect. Both participants had a larger head circumference than female participants. Therefore, a pure ‘power’ hypothesis does not account for the observed pattern of results here.

Secondly, the size of other brain structures has been found to depend on gender: Frederikse, Lu, Aylward, Barta, and Pearlson (1999) have shown that the inferior parietal lobe is larger in males than in females. Thus it may be possible that the impact of rTMS on cognitive functions that are supposed to rely on the PC is negatively correlated with the size of the stimulated areas. According to Hatta, Kawakami, Kogure, and Itoh (2002; see also Ratinckx et al., in press) this should hold for situations when interhemispheric collaboration does not provide any benefit, i.e. when the task at hand is simple. Under these circumstances the processing capacities provided by the dominant hemisphere should suffice to solve the task. While Dehaene et al. (2003) postulate a bilateral representation of numerical magnitude some evidence suggests a relative left hemispheric dominance (e.g. Lemer et al., 2003; Sandrini et al., 2004; Cohen Kadosh et al., 2005), especially with respect to a precise numerical magnitude judgement (cf. Andres et al., 2005). Thus, the impact of
rTMS on the LH may not have been strong enough for male participants to affect both the left-hemispheric and the right-hemispheric hIPS to a sufficient degree. Thereby, the right hemispheric hIPS with its more holistic (approximate) processing style may have taken over the two-digit magnitude comparison task to a greater extent. As laid out above, this may have led to a decrease in the distance effect with TMS. Additionally, this might also lead to a relative decrease in the compatibility effect. In contrast, for male participants we did not only observe a null effect, but a numerical decrease of the compatibility effect which seemed to be similar in size to the decrease in the distance effect. Thus a potential benefit of TMS – its spatial focality – may have influenced the results in this study in a characteristic way which was gender specific.

To sum up, supportive evidence for the claim that susceptibility for TMS depends on gender was found. Moreover, Study 3 suggests that morphological (gender) differences might mediate the impact of TMS on performance in a paradigm of higher cognitive functions.

To conclude, the results of this TMS study corroborate numerous fMRI studies postulating an important impact of areas around the hIPS for number processing (e.g. Dehaene et al., 2003; Hubbard et al., 2005 for an overview). This TMS study is among the first to demonstrate the functional relevance of the hIPS for number magnitude processing by showing modulation of within-task magnitude-related effects. In Study 3, not only general task performance (as measured by RT or errors) was modulated by TMS, but also the most important index of numerical magnitude activation, namely, the distance effect. In addition, Study 3 indicates that the hIPS also plays a functional role in the integration of the single digits in two-digit number magnitude comparison. These effects were, however, modulated by gender. In line with previous research in other domains, it is argued that gender-specific differences in TMS studies may be due to gender-specific susceptibility for the TMS signal. Since the TMS modulations partially went into opposite directions for males and females, previous lack of modulation, for instance for the distance effect, may have been due to the mixed (and small) samples of men and women.

Finally, since two different cognitive effects being differentially related to number processing were investigated, the results can serve to further specify the functional role of the hIPS in the course of number processing. The interpretation of the TMS results is in line with a more holistic processing style in the right hemisphere and a more decomposed processing style in the left hemisphere. It is concluded that studying the differential involvement of both hemispheres and their different numerical processing styles may help to understand functioning and impairments of number processing and calculation in the future.
5 Study 4

A Special Role for Numbers in Working Memory? – An fMRI Study.

Published in Neuroimage, 29: 1 – 14.

(Co-authored with H.-C. Nuerk, B. Fimm, R. Vohn, and K. Willmes)
5.1 Introduction

While the majority of vWM studies employ letters as stimuli several vWM studies utilize numbers (e.g. Corbetta et al., 2002; Coull & Frith, 1998; Kondo et al., 2004; Landro et al., 2001). If stimulus specific (i.e. numbers versus letters) or task specific activations exist, results of different vWM studies employing different stimuli or tasks should only be compared with one another with great care.

The present study was designed to investigate the influence of different tasks and different stimulus materials on parietal activation in a WM context: Among other studies, Study 2 and Study 3 suggest a fundamental contribution of the parietal cortex to the processing of numerical magnitude information. If presenting numbers induces additional parietal activation in the hIPS as compared to non-numerical stimulus material, this can be interpreted as stimulus-specific modulation of activity in PC. Moreover, it casts some doubt on purely phonological processing in verbal WM, because this modulation has its origin in averbal stimulus attributes.

In addition, we examine the influence of task on activity in PC. We compare a task explicitly addressing magnitude or sequence information (comparison task, see below) with a task that does not require such a representation (identity match task).
5.2 Methods

5.2.1 Participants

16 healthy male persons (mean age = 27.0 years; SD = 7.65 years) participated in the study. Written informed consent was obtained prior to the start of the scanning session. The project was approved by the local Ethics Committee of the Medical Faculty RWTH Aachen University. Participants were given the opportunity to practice each task condition once in a separate room to familiarize them with the task. Three subjects had to be discarded from the analysis because of technical problems with the response button interface or with the head mounted video goggles. Thus, all analyses are based on data from 13 participants.

5.2.2 Stimuli

Numbers (1, 4, 6, 9) and letters (B, K, M, X) were centrally presented in red colour. The stimuli extended to 4.5° vertical angle and 2.9° horizontal angle. In order to avoid afterimages, each stimulus was followed by a mask which was composed of several rectangles of different size. In order to avoid semantic and structural influences of multi-digit numbers (cf. Nuerk et al., 2001), we restricted our stimulus material to one-digit numbers. Dehaene and colleagues (1993) have demonstrated that a given number's relative magnitude is estimated with regard to the range of stimuli used for the experiment. That is, the number five elicits relatively faster responses with the right hand than with the left hand in a magnitude comparison task (SNARC effect: Spatial Numerical Association of Response Codes) when stimuli range from 0 to 5 but pattern of responses is vice versa when stimuli range from 4 to 9 (also Fias et al., 1996). Thus, we made stimulus ranges comparable between one-digit numbers and letters by choosing stimuli from the entire range possible for each type of stimulus material (one-digit numbers and letters). Note that a SNARC effect has been observed in tasks using letters as stimulus material implying that letters convey at least some major properties with the numerical dimension in that some magnitude or sequence representation is activated automatically and capable of biasing manual responses (Gevers et al., 2003). Still, numbers differ from letters in terms of their scale properties: While letters can only be compared with regard to their sequential order, numbers allow for computations and manipulations such as e.g. addition, subtraction and numerical comparison. For numbers comparison can both relate to their cardinal (magnitude comparison) or ordinal properties (sequential order comparison). Henceforth we use the term "comparison task" as the generic term for the different types of comparison in the different stimulus types.
5.2.3 Procedure

We made use of an n-back paradigm using letters (verbal) and numbers (averbal/numerical) as memoranda (henceforth L and N). The n-back paradigm offers the opportunity to vary orthogonally stimulus material and task for different WM loads. It consists of a series of single stimuli presented visually to participants who have to press one button if the actual stimulus matches (Identity Match, henceforth I) a stimulus shown n-trials prior, and another if not. We also introduced a second kind of task for the n-back paradigm in order to specifically activate a magnitude/ alphabetical sequence representation: Instead of asking whether a stimulus is identical to a stimulus shown n trials prior we asked participants to judge whether the actual stimulus is “smaller” or “larger” than the one shown n trials before (Comparison Task, henceforth C). To keep tasks as comparable as possible, participants were instructed to refer to the alphabetical sequence when deciding on the relative “magnitude” (i.e. their alphabetical position) of letters (A < B etc.). This was clarified by an example given by the experimenter.

Three levels of memory load (lag 0 [L0], lag 1 [L1] and lag 2 [L2]) were presented in a factorial design fully crossed with levels of stimulus type and task. This resulted in 12 different conditions each presented three times adding up to a total of 36 conditions. The order of the different conditions was pseudo-randomized in order to control for potential sequence effects. Increasing memory load within each task by stimulus material combination was held constant.

In the identity match task participants had to decide if the stimulus shown matched (a) either of two previously defined standards (1 or 6 for NIL0, and B or M for LIL0), (b) the stimulus shown before (NIL1 or LIL1) or (c) the last but one stimulus (NIL2 or LIL2). Comparison task required a decision whether (a) the stimulus shown was “smaller” or “larger” than 5 (NCL0) or L (LCL0), (b) the stimulus shown was “smaller” or “larger” than the one shown in the trial before (NCL1 or LCL1) or (c) the stimulus shown was “smaller” or “larger” than the stimulus presented two trials before (NCL2 or LCL2). In lag 0 of the identity match task, subjects had to indicate the occurrence of either of both standards as soon as possible.

In order to prevent alternative strategies and response biases solely due to the fact that no stimulus could be “smaller” (“larger”) than 1 or B (9 or X), two (three) catch trials per block were included for lag 1 and lag 0 (lag 1). Thus catch trials contribute 12.5% (18.75%) of the total number of trials in lag 0 and lag 2 (lag 1). Catch trials consisted of identical stimuli on the corresponding position within the sequence of stimuli together with the instruction to respond “identical” rather than “smaller” or “larger”. Therefore we additionally presented the number 5 (the letter L) in the NCL0 (LCL0) conditions. With the exception of the first trial in the L1 condition and the first two trials in the L2 condition, where no response had to be given at all, in each trial participants were to respond either with their left hand (“smaller”/“not identical”),
right hand ("larger"/"identical") or both hands (catch trials) pressing a pneumatic response button.

A condition started with a resting phase for 14.5 sec. followed by a written instruction for 4 sec. that informed participants about task requirements and response button assignment. After a short delay of 500ms the condition/task was started. Each condition lasted approximately 65 seconds and consisted of a sequence of 14 stimuli. Each stimulus was presented for 2100ms followed by the mask. The mask was shown for 800ms after which the screen turned black for 50ms. 6 functional conditions formed a subsession which lasted approximately 6 minutes. The whole experimental procedure contained 6 subsessions and lasted approximately 45 minutes.

Stimuli were presented via a head mounted video display (http://www.mrivideo.com) designed to meet MR requirements. Vision was corrected to normal if necessary by inserting adapting lenses in the goggles.

5.2.4 MRI Scanning Procedure

Images were acquired at the University Hospital of the RWTH Aachen University, using a 1.5T Philips Gyroscan NT with standard head coil and foam padding to restrict movements. Axial multisclice T2*-weighted images were obtained with a gradient-echo planar imaging sequence (TE = 50ms; TR = 3 sec.; 64 X 64 matrix; flip angle = 90°; 30 slices, 3.4375 X 3.4375mm in-plane resolution; slice thickness 4mm; no gap), covering the entire brain. During each subsession 132 volumes were acquired. Each subsession started with 3 dummy scans that were not recorded for data analysis to allow tissue to reach steady state magnetization.
5.3 Results

5.3.1 Behavioural Data

Reaction Time (RT) analysis was based on correct trials only. The trimming procedure excluded RTs outside 3 SD around a participant’s average. RT was analyzed via a 2 X 2 X 3 repeated measures analysis of variance (ANOVA) comprising the factors stimulus material (numbers vs. letters), task (identity match vs. comparison) and lag (0 to 2).

Main effects were present for all three factors. Numbers were responded to faster than letters (883 ms vs. 920 ms; F(1, 12) = 12.51; p < .01). Identity match yielded faster responses than comparison (866 ms vs. 936 ms; F(1, 12) = 27.52; p < .01). Participants responded faster on lag 0 than on lag 1 which in turn was responded to faster than lag 2 (773 ms vs. 825 ms vs. 1129 ms; F(2, 24) = 121.2; p < .01 for the main effect and t(12) = -3.13; p < .01; t(12) = -10.6; p < .01 for pairwise comparisons between adjacent lags). All interactions were statistically reliable.

Task interacted significantly with stimulus material (F(1, 12) = 34.60; p < .01): While for numbers RT in identity match did not differ from comparison (t(12) = -.75; p > .4), for letters responses were faster in the identity match (860 ms) than in the comparison condition (994 ms; t(12) = -6.96; p < .01). Stimulus material only marginally affected RT when participants had to match identity (F(1, 12) = 3.49; p < .1): Letters were responded to faster than numbers (860 ms vs. 886 ms). For the comparison task, letters were responded to more slowly than numbers (994 ms vs. 897 ms; F(1, 12) = 44.02; p < .01).

Task interacted with WM load (F(2, 24) = 17.13; p < .01). While task had no influence depending on WM load in lag 0, in lag 1 and lag 2 participants responded faster when matching identity (805 ms and 1053 ms) than when they had to compare items with each other (844 ms and 1205 ms; t(12) = -2.19; p < .05 and t(12) = -6.50; p < .01). Thus, the comparison task was more difficult for high WM load than the identity match task.

WM load interacted with stimulus material (F(2, 24) = 9.49; p < .01). For low WM load conditions (lag 0 and lag 1) participants were faster when numbers had to be processed (lag 0: 734 ms vs. 812 ms; lag 1: 794 ms vs. 855 ms; t(12) = -4.43; p < .01; and t(12) = 3.44; p < .01), but the difference between numbers and letters on lag 2 conditions (1147 ms vs. 1112 ms) was statistically not reliable (p > .1).

The three-way interaction was also significant (F(2, 24) = 12.56; p < .01) indicating that stimulus material and task differentially affected processing with increasing WM load. As identity match is the task most often used in WM studies we analyzed both tasks separately. In the identity match task, stimulus material did not interact with varying WM load (p > .65). However, in the comparison task WM load significantly interacted with stimulus material (F(2,
While for low WM load (lag 0 and lag 1) numbers were responded to faster than letters (689 ms vs. 886 ms; t(12) = -5.97; p < .01 and 776 ms vs. 912 ms; t(12) = -5.48; p < .01), stimulus material did not produce significant effects for WM load (letters: 1183 ms vs. numbers: 1227 ms; p > .15).

Figure 24: RT (lines) and ER (bars) for letters (grey colour) and numbers (black colour) for identity match and comparison task, and all lags (lag 0, lag 1 and lag 2). Error bars indicate standard errors.

Error rate (ER) data include false responses and misses. Error rates were arcsine-transformed before a three-way repeated measures ANOVA again comprising the factors task (2), stimulus type (2), and lag (3) was carried out. For reason of illustration we report original error probabilities in Figure 24. There were statistically reliable main effects of task (F(1, 12) = 89.47; p < .01), stimulus material (F(1, 12) = 6.04; p < .05), and lag (F(1, 12) = 16.02; p < .01). Participants made more errors (a) when responding to numbers as compared to letters (13.6 % vs. 12.7%) and (b) in the comparison task as compared to identity match (20.4% vs. 5.9%). Error rate monotonically increased with increasing WM load (lag 0 = 7.9%; lag 1 = 13.8%; lag 2 = 17.8%).
Task interacted significantly with type of stimulus material ($F(1, 12) = 14.91; p < .01$), i.e. while for identity match letters caused less errors than numbers ($5.2\%$ vs. $7.6\%; t(12) = -4.01; p < .01$), this difference was absent for the comparison task ($21.3\%$ vs. $19.6\%)$. This is at variance with the results from RT data (numbers were responded to faster than letters in the comparison task) and might be taken as an indication for a speed accuracy trade off for numbers in this task. No other interaction reached significance.

RT and ER data implicate that participants fulfilled task demands, since a clear effect of WM load was present in all 4 stimulus type by task conditions. Thus we were successful in stimulating WM processes. Overall, the comparison task was performed more slowly and led to more errors than identity match task. In detail, it seems that comparison was more difficult for letters than for numbers but only at low memory loads while for high WM load the stimulus material no longer affected performance in this task differentially. The complexity of this pattern of results suggests that information processing within WM depends on the material presented, the task to be carried out and on the interaction of these two factors. Numbers differ from letters only when the task at hand explicitly requires comparison and WM load is low. Performance in the comparison task with high WM load (lag 2) and numbers as memoranda might be interpreted in terms of semantic interference that arises when intermediate numerical representations have to be overruled in order to compare two numbers to each other. However, since this is the only possible indication of some sort of semantic processing of numbers in a WM context, evidence for averbal semantic processing in vWM is scarce.

5.3.2 Imaging Data

Functional images were analyzed with statistical parametric mapping software (SPM2; http://www.fil.ion.ucl.ac.uk/spm/spm2.html). Images were motion corrected and realigned to each participant’s first image. No participant had to be discarded from further analysis because of movement artefacts exceeding a limit of one voxel size per axis. Data were normalized into standard stereotactical space. Spatial smoothing was performed on the normalized functional images using a Gaussian kernel of 12 mm FWHM.

The effects of interest were assessed for each participant separately and were submitted to a random effects group analysis. To test for consistency of participants’ activation we conducted one sample t-tests on constraint estimates. Results are reported in accordance with the questions raised in the introduction. Since some of the computed contrasts are very close in terms of processing requirements - i.e. the expected effects are rather small - no correction for multiple comparisons has been carried out. Type-I-error level was set to $p < .05$. In contrast, the activation pattern elicited by increasing WM load was tested more conservatively with a correction for multiple comparisons (False Discovery Rate
Except for ROI analyses, the threshold was set to a minimum of 10 adjacent voxels to be activated. Regions of interest were chosen on the basis of the meta-analysis by Dehaene and colleagues (2003). The authors report mean coordinates which serve as the most likely location of the neural correlate of number magnitude representation. These coordinates are (-44, -48, 47) for the left and (41, -47, 48) for the right hemisphere (LH/RH) which are located around the horizontal aspects of the IPS. The form of the ROIs was that of a box which extended to a size of 7, 5, and 6mm for left ROI, and 7, 7, and 5mm for right ROI in x, y, z-direction, respectively. These values are identical to the standard deviations of the coordinates reported by Dehaene et al. (2003). Given that the centres of activation are distributed normally, 68% of activated voxels fall within this range. Activations outside the ROIs are reported for reasons of comprehensiveness.

**Working Memory**

In order to assess in which brain areas activity correlates with increasing WM load we contrasted L2 – L1, masked inclusively by corresponding contrasts for each stimulus material separately (i.e. LL2 – LL1 and NL2 – NL1). This was done to reveal the WM load specific aspects that are common to both stimulus materials. In the remaining description of results we concentrate on these contrasts when we refer to WM load, because with regard to task demands lag 1 is more comparable to lag 2 than lag 0 is: While in lag 0 participants do not have to change the standard they compare the actual stimulus to, this is well the case in lag 1 and lag 2 conditions. This offers good comparability of task requirements of lag 1 and lag 2 with regard to the need of continuously updating the content of working memory. In line with previous studies utilizing an n-back paradigm to assess WM we observed a network comprising bilateral PFC (Brodmann Area (BA) 46), bilateral PC (BA 40) extending into the precuneus (BA 7), and supplementary motor area (SMA, BA 6), bilaterally (see Figure 25). In a number specific contrast (NL2 – NL1) the cingulate gyrus (TC: -8, 22, 43; BA 32) was activated additionally. Centres of activations for inclusively masked main effect of vWM load (L2 – L1) are given in Table 11.
Figure 25: WM-load specific activity (L2 – L1, FDR-corrected, p < .01) masked inclusively with the corresponding contrast for each stimulus material separately [(NL2 – NL1) and (LL2 – LL1); p < .05, uncorrected]. The observed activation pattern was consistent with WM-related network showing bilateral DLPFC and PC activation.

Table 11: WM load related activations (lag 2 – lag 1) masked inclusively with stimulus material specific WM load contrasts (NL2 – NL1 & LL2 – LL1)

<table>
<thead>
<tr>
<th>Contrast</th>
<th>Brain Region (BA)</th>
<th>TC (x, y, z)</th>
<th>Cluster Size</th>
<th>Z - Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>lag 2 – lag 1</td>
<td>LH Superior Frontal Gyrus (11)</td>
<td>-24 46 -16</td>
<td>19</td>
<td>4.39</td>
</tr>
<tr>
<td></td>
<td>LH Medial Frontal Gyrus (8)</td>
<td>-8 22 43</td>
<td>20</td>
<td>3.64</td>
</tr>
<tr>
<td></td>
<td>LH Medial Frontal Gyrus (8)</td>
<td>-1 18 48</td>
<td></td>
<td>3.54</td>
</tr>
<tr>
<td></td>
<td>LH Middle Frontal Gyrus (46)</td>
<td>-44 25 25</td>
<td>454</td>
<td>5.62</td>
</tr>
<tr>
<td></td>
<td>LH Middle Frontal Gyrus (6)</td>
<td>-40 7 55</td>
<td></td>
<td>4.49</td>
</tr>
<tr>
<td></td>
<td>LH Inferior Frontal Gyrus (46)</td>
<td>-44 43 5</td>
<td></td>
<td>4.42</td>
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<tr>
<td></td>
<td>RH Middle Frontal Gyrus (46)</td>
<td>51 36 20</td>
<td>519</td>
<td>4.90</td>
</tr>
<tr>
<td></td>
<td>RH Middle Frontal Gyrus</td>
<td>44 32 17</td>
<td></td>
<td>4.80</td>
</tr>
<tr>
<td></td>
<td>RH Middle Frontal Gyrus</td>
<td>28 10 51</td>
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<td>4.79</td>
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<td></td>
<td>RH Insula (13)</td>
<td>32 20 3</td>
<td>10</td>
<td>4.29</td>
</tr>
<tr>
<td></td>
<td>RH Inferior Parietal Lobe (40)</td>
<td>36 -49 39</td>
<td>851</td>
<td>6.24</td>
</tr>
<tr>
<td></td>
<td>LH Inferior Parietal Lobe (40)</td>
<td>-36 -45 39</td>
<td></td>
<td>5.32</td>
</tr>
<tr>
<td></td>
<td>RH Superior Parietal Lobe (7)</td>
<td>40 -60 51</td>
<td></td>
<td>5.10</td>
</tr>
<tr>
<td></td>
<td>LH Middle Occipital Lobe (19)</td>
<td>-32 -78 4</td>
<td>13</td>
<td>3.74</td>
</tr>
<tr>
<td></td>
<td>RH Cerebellum</td>
<td>0 -48 -18</td>
<td>71</td>
<td>4.12</td>
</tr>
<tr>
<td></td>
<td>LH Cerebellum</td>
<td>-16 -75 -20</td>
<td>18</td>
<td>3.59</td>
</tr>
</tbody>
</table>

Note. FDR corrected p < .05; cluster size ≥ 10 Voxels; masks were created at uncorrected p < .05; N – number; L – letter; L1 – lag 1; L2 – lag 2; BA – Brodman area; TC – Talairach coordinates; LH – left hemisphere; RH – right hemisphere;

Analyzing each stimulus material X task combination separately reveals a largely coherent network of activations that resembles very well the often reported WM related
network comprising PFC, PC and ACC. Stimulus specific WM activity for both numbers and letters is superimposed in Figure 26A for identity match task. Figure 26B shows activity for letter and number specific WM activity in the comparison task. Letter specific activity is shown in red, number specific activity is depicted in green. Brain structures activated by both materials are indicated by yellow colour. Centres of activations are described in Table 12.

Figure 26: Superimposed contrasts (FDR-corrected, p < .05) for letter X task specific WM load (lag 2 – lag 1). Letters specific activity is shown in red, number specific activity is shown in green. Brain areas activated by both stimulus materials are shown in yellow. (A) WM activity for identity match task [(LIL2 – LIL1): red; (NIL2 – NIL1): green] (B) WM activity for the comparison task [(LCL2 – LCL1): red; (NCL2 – NCL1): green].
### Table 12: Maxima (and 1 minor maxima) of working memory load activity (lag 2 – lag 1) for each stimulus material X task condition separately

<table>
<thead>
<tr>
<th>Contrast</th>
<th>Brain Region (BA)</th>
<th>TC (x, y, z)</th>
<th>Cluster size</th>
<th>Z -Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>LCL2 – LCL1</td>
<td>RH Middle Frontal Gyrus (9)</td>
<td>40 24 21</td>
<td>547</td>
<td>4.42</td>
</tr>
<tr>
<td></td>
<td>LH Middle Frontal Gyrus (46)</td>
<td>-51 29 28</td>
<td>295</td>
<td>4.28</td>
</tr>
<tr>
<td></td>
<td>RH Medial Frontal Gyrus (8)</td>
<td>4 25 43</td>
<td>27</td>
<td>3.33</td>
</tr>
<tr>
<td></td>
<td>LH Fusiform Gyrus (19)</td>
<td>-32 -79 -16</td>
<td>179</td>
<td>3.81</td>
</tr>
<tr>
<td></td>
<td>LH Precuneus (7)</td>
<td>-28 -65 29</td>
<td>352</td>
<td>4.63</td>
</tr>
<tr>
<td></td>
<td>RH Inferior Parietal Lobe (40)</td>
<td>36 -49 39</td>
<td>351</td>
<td>4.47</td>
</tr>
<tr>
<td></td>
<td>RH Brainstem</td>
<td>4 -20 -16</td>
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<td>LIL2 – LIL1</td>
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<td></td>
<td>LH Middle Frontal Gyrus (6)</td>
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<tr>
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<td>RH Middle Frontal Gyrus (6)</td>
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<td></td>
<td>RH Middle Frontal Gyrus (46)</td>
<td>51 32 28</td>
<td>37</td>
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<tr>
<td></td>
<td>RH Middle Frontal Gyrus (10)</td>
<td>44 51 12</td>
<td>14</td>
<td>3.86</td>
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<tr>
<td></td>
<td>RH Superior Frontal Gyrus (10)</td>
<td>28 58 -10</td>
<td>27</td>
<td>4.38</td>
</tr>
<tr>
<td></td>
<td>LH Superior Parietal Lobe (7)</td>
<td>-24 -64 40</td>
<td>60</td>
<td>3.65</td>
</tr>
<tr>
<td></td>
<td>RH Inferior Parietal Lobe (40)</td>
<td>32 -49 36</td>
<td>139</td>
<td>4.59</td>
</tr>
<tr>
<td>NCL2 – NCL1</td>
<td>LH Middle Frontal Gyrus (9)</td>
<td>-48 21 36</td>
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<td>4.36</td>
</tr>
<tr>
<td></td>
<td>RH Middle Frontal Gyrus (6)</td>
<td>28 3 51</td>
<td>15</td>
<td>3.58</td>
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<td>LH Inferior Frontal Gyrus (?)</td>
<td>-40 43 2</td>
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<td>3.86</td>
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<tr>
<td></td>
<td>RH Inferior Parietal Lobe (40)</td>
<td>36 -52 43</td>
<td>32</td>
<td>4.10</td>
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<td>LH Inferior Parietal Lobe (40)</td>
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<td>4.69</td>
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<td>LH Superior Parietal Lobe (7)</td>
<td>-28 -63 55</td>
<td>61</td>
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<tr>
<td>NIL2 – NIL1</td>
<td>RH Middle Frontal Gyrus (6)</td>
<td>28 10 47</td>
<td>136</td>
<td>5.38</td>
</tr>
<tr>
<td></td>
<td>RH Middle Frontal Gyrus (46)</td>
<td>48 36 20</td>
<td>74</td>
<td>3.83</td>
</tr>
<tr>
<td></td>
<td>RH Middle Frontal Gyrus (10)</td>
<td>32 58 10</td>
<td>10</td>
<td>3.40</td>
</tr>
<tr>
<td></td>
<td>LH Inferior Frontal Gyrus (9)</td>
<td>-48 1 22</td>
<td>710</td>
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<td>LH Medial Frontal Gyrus (8)</td>
<td>-4 25 43</td>
<td>27</td>
<td>4.02</td>
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<tr>
<td></td>
<td>LH Inferior Frontal Gyrus (10)</td>
<td>-40 51 1</td>
<td>71</td>
<td>4.47</td>
</tr>
<tr>
<td></td>
<td>RH Middle Temporal Gyrus (39)</td>
<td>36 -68 29</td>
<td>215</td>
<td>4.42</td>
</tr>
<tr>
<td></td>
<td>(RH Inferior Parietal Gyrus (40))</td>
<td>44 -60 44</td>
<td>4.32</td>
<td></td>
</tr>
<tr>
<td></td>
<td>LH Middle Temporal Gyrus (37)</td>
<td>-40 -58 -4</td>
<td>15</td>
<td>3.33</td>
</tr>
<tr>
<td></td>
<td>LH Lentiform Nucleus</td>
<td>-20 -4 0</td>
<td>18</td>
<td>3.83</td>
</tr>
<tr>
<td></td>
<td>RH Anterior Lobe (Cerebellar Lingual)</td>
<td>4 -43 -15</td>
<td>50</td>
<td>4.23</td>
</tr>
</tbody>
</table>

Note. FDR corrected p < .05; cluster size ≥ 10 Voxels; BA – Brodman area; TC – Talairach coordinates; N – number; L – letter; I – identity match task; C – comparison task; L1 – lag 1; L2 – lag 2; RH – right hemisphere; LH – left hemisphere
Material Specific Activity

Subtracting letters from numbers in corresponding conditions yields activation that can be attributed to number related processes or representations. With respect to the hIPS, results are summarized in Table 13. The subtraction of letter conditions from number conditions (N – L), irrespective of other factors and masked inclusively with task specific contrasts (NI – LI & NC – LC) did not reveal any activation in the ROIs (see Table 3). Only left precentral cortex (BA 4 & 6) showed significant activation. Neither did contrasting numbers to letters, separately for each task but concatenated over lags (NI – LI & NC – LC) reveal any significant activity in hIPS. Rather, for contrast NM – LM a network of activity was observed, consisting of left precentral gyrus (BA 6), bilateral cingulate cortex (BA 32), extending to the middle frontal gyrus, left middle and superior temporal gyrus (BA 39 and BA 38, respectively), parahippocampal gyrus (BA 22), and right nucleus caudate. Contrasting NI against LI revealed activity in left inferior and superior frontal gyrus (BA 47 and BA 6, respectively), part of which extended into precentral and postcentral gyri (BAs 3, 4, 43) left middle frontal gyrus (BA 11), right fusiform gyrus (BA 37), right inferior parietal gyrus (BA 40), as well as cuneus (BAs 31 & 18).

We further analyzed data by disentangling number specific contributions to both tasks and each lag. Bilateral hIPS activation was only found contrasting NIL1 vs. LIL1 (see Table 13; p < .05, uncorrected).

Absence of increased activity can be due to at least two reasons: First, there were no activations within this region at all, and second they were cancelled out by subtraction. Thus, in order to clarify involvement of the IPS in WM, we analyzed ROI activation by contrasting each experimental condition against rest: We found the hIPS to be significantly activated in all contrasts (FDR corrected; p < .01).

The hIPS was clearly involved in solving the WM task in all conditions. Increased involvement of hIPS was found only in contrast (NIL1 – LIL1). The main effect was not significant. Thus, numbers did not consistently increase brain activity in IPS when compared to letters as stimulus material in this WM context.
**Table 13:** Stimulus material specific activity in hIPS as (i) main effect, (ii) separately for each task, and (iii) separately for each task X WM load combination

<table>
<thead>
<tr>
<th>Identity Match Task</th>
<th>hIPS activity</th>
<th>Comparison Task</th>
<th>hIPS activity</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>NIL1 – LI1</td>
<td>BH: -44, -40, 46</td>
</tr>
<tr>
<td></td>
<td>-</td>
<td>NCL0 – LCL0</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>NIL2 – LI2</td>
<td>BH: -44, -40, 46</td>
</tr>
<tr>
<td></td>
<td>-</td>
<td>LCL2 – LCL2</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>LIL0 – NIL0</td>
<td>BH: -44, -44, 46</td>
</tr>
<tr>
<td></td>
<td>-</td>
<td>LCL0 – NCL0</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>LIL1 – NIL1</td>
<td>BH: -44, -48, 50</td>
</tr>
<tr>
<td></td>
<td>-</td>
<td>LCL1 – NCL1</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>LIL2 – NIL1</td>
<td>BH: -44, -44, 46</td>
</tr>
<tr>
<td></td>
<td>-</td>
<td>LCL2 – NCL2</td>
<td></td>
</tr>
</tbody>
</table>

**Main effect contrasts**

<table>
<thead>
<tr>
<th>hIPS activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Numbers – Letters</td>
</tr>
<tr>
<td>-</td>
</tr>
<tr>
<td>Letters – Numbers</td>
</tr>
<tr>
<td>-</td>
</tr>
</tbody>
</table>

Note. ROI had the form of a box extending 7mm, 5mm, and 6mm (LH), and 7mm, 7mm, and 5mm (RH) into x, y, and z dimension, respectively. The centre was located at Talairach coordinates (-44, -48, 47) for the LH and (41, -47, 48) for the RH. hIPS – horizontal aspects of the intraparietal sulcus; N – number; L – letter; I – identity match task; C – comparison task; L0 – lag 0; L1 – lag 1; L2 – lag 2; BH – both hemispheres; LH – left hemisphere; RH – right hemisphere
Letter specific activity

Though not being the major topic of the present study we investigated which brain areas were activated by letters more than by numbers. In contrast to number related brain activity we did not have any specific hypotheses about which areas would be activated more by letters than by numbers. Thus we describe all brain areas activated before taking a closer look at the ROIs.

The main effect of letters as compared to numbers (L – N), masked inclusively by (LI – NI & LC – NC) revealed a network of activations including right precentral gyrus (BA 4), right middle frontal gyrus (BA 9), and lingual gyrus (BA 18 for RH and BA 17 for LH), bilaterally. No hIPS activity was present. Analyzing each task separately revealed the following results: For identity match (LI – NI) bilateral activity was observed in middle frontal gyrus (BA 46), superior temporal gyrus (BA 38), posterior cingulate gyrus (BA 30), and occipital lobe (BA 18). Additionally, right precentral gyrus (BA 6), superior frontal gyrus (BA 9/11), and precuneus (BA 7), as well as left superior frontal gyrus (BA 10) were significantly activated. Again, no hIPS activity was observed.

A widespread network of activity was also found for the comparison task specific contrast of letters vs. numbers (LC – NC): Right hemispheric activity was found in middle and inferior frontal gyrus (BA 9, 11), superior temporal gyrus (BA 37), supplementary and primary motor cortex (BA 6, 5) and postcentral gyrus (BA 1/2/3), extending into parietal cortex (BA 40). Left hemispheric activity was found in premotor cortex (BA 6), inferior frontal gyrus and insula (BA 13), middle frontal gyrus (BA 10/46), subcallosal gyrus (BA 25), and precuneus (BA 7). Occipital lobe was active bilaterally (BA 17/18/19). Bilateral activity was observed in the ROI analysis, with RH activity being slightly more pronounced than LH activity.

Analyzing each condition separately did not reveal consistently increased activity within the ROI. Contrasting letters against numbers in the comparison task yielded bilateral hIPS activity in contrasts LCL0 – NCL0, and LCL2 – NCL2.

Summing up, using letters instead of numbers in a WM task only induces additional activity in the hIPS in the comparison task with either high (i.e. lag 2) or low (i.e. lag 0) WM load. The identity match task does not induce additional activity in hIPS when compared to numbers as stimulus material.

Taken together, as far as material specific effects are concerned, the hIPS did not reveal a great amount of number specific activation but was recruited by both stimulus materials in the context of a WM task. If any, letters had a stronger impact in our ROI, incompatible with the view that hIPS activity is stimulus material or even number specific (Eger et al., 2003). Letter specific activity was restricted to the comparison task, i.e. conditions in which it is very likely that a mental magnitude/sequence representation is accessed by the participants.
Task Demands

Analyses of task specific activities were computed subtracting one task from the other (i.e. C – I and I – C) and masking results inclusively by stimulus material specific task related activity [(NC – NI & LC – LI), and (NI – NC & LI – LC), respectively]. Results are summarized in Table 14.

Contrasting comparison task against identity match task (C – I masked inclusively by LC – LI, and NC – NI with p = .05, uncorrected both for mask and contrast of interest) revealed bilateral activity in the precuneus (BA 7/19) extending into superior parietal areas (BA 7) in the left hemisphere and into the middle temporal gyrus (BA 39) in the right hemisphere.

When contrasting the identity match task against the comparison task (I – C) activity in medial frontal gyrus (BA 6, 9), middle temporal gyrus (BA 21), postcentral gyrus (BA 2) and cingulate gyrus (BA 24, 31) was found. The ROI did not show significantly increased activity.

In order to test the hypothesis of increased hIPS activity induced by explicitly referring to the magnitude/alphabetical position of the stimulus we contrasted the identity match task against the comparison task, individually for each stimulus material and pooled over all lags (NC – NI):

The hIPS was not active in contrast NC – NI whereas a significant amount of activity was observed in the right hIPS (p < .05, uncorrected) when contrasting NI – NC. In addition, for number specific task demands comparison in contrast to identity match significantly activated anterior (BA 24/32) and posterior (BA 23) cingulate gyrus (BA 24/32), and superior temporal gyrus, bilaterally (BA 38/39 for LH and BA 38 for RH). The opposite comparison (NC – NI) revealed activity in right medial and middle frontal gyrus (BA 47 and BA 10), bilateral precentral gyrus (BA 6 & 4), bilateral superior temporal gyrus (BA 41 for LH & BA 38 for RH), bilateral insula (BA 13), anterior cingulate (BA 32), thalamus, caudate, left postcentral gyrus (BA 3), and left middle as well as inferior occipital gyrus (BA 18 & 17), extending into the lingual gyrus (BA 18).

For letters the influence of task was reverse: bilateral hIPS activity was observed in contrast LC – LI while no ROI activity was present in contrast LI – LC (see Table 14). Contrasting LC vs. LI revealed a left lateralized (pre-)frontal network comprising precentral (BA 6/4) and middle frontal gyrus (BA 47/10). Right (pre-)frontal cortex did not reveal any additional activity as compared to the identity match task, except small clusters of activity in the medial frontal gyrus (BA 8) extending into the cingulate gyrus (BA 32), parahippocampal gyrus (BA 34), and lentiform nucleus. Left lateralized activity in occipital cortex (BA 18) was found. No activity was present in contrast LI – LC.

Contrasting corresponding conditions (while keeping WM load and stimulus material constant) only differing with regard to the task revealed the following results: Bilateral
activation was found in the hIPS when contrasting LCL0 vs. LIL0. Left lateralized hIPS activity was observed in contrasts LCL1 – LIL1, and LCL2 - LIL2 (see Table 14). No contrast involving numbers in comparison vs. identity match revealed activation in our ROI. In contrast, RH showed activity in the hIPS in contrasts NIL1 – NCL1, and NIL2 – NCL2.

Following Dehaene and colleagues (2003), explicitly addressing magnitude representation/sequential order information in a WM task should induce additional activity in hIPS. However, for number specific contrasts (NI – LI, NIL1 – NCL1 and NIL2 – NCL2) the opposite was true, hence speaking against this hypothesis. When letters were used as stimulus material explicitly addressing sequential order information did induce additional activity in the hIPS (LC – LI, LCL0 – LIL0, LCL1 – LIL1, and LCL2 – LIL2) that might be attributed to activating the mental order representation.

Taken together, it was not the task alone that determined activation in the hIPS but an interaction of task and stimulus material. The comparison task did additionally activate hIPS in the LH but no such additional impact was present when numbers were used as stimulus material. In letter conditions however, comparison lead to increased hIPS activation when contrasted to identity match. Increased activity in the hIPS cannot solely be attributed to enhanced access to the magnitude/sequential order representation due to the comparison task since identity match (NIL0 – NCL0 and NIL2 – NCL2) evoked additional activity in hIPS, too.
Table 14: Task specific activity in hIPS as (i) main effect, (ii) separately for each stimulus material, and (iii) separately for each stimulus material X WM load combination

<table>
<thead>
<tr>
<th>Numbers</th>
<th>Letters</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Contrast</strong></td>
<td><strong>hIPS activity</strong></td>
</tr>
<tr>
<td>NC – NI</td>
<td>-</td>
</tr>
<tr>
<td>NCL0 – NIL0</td>
<td>-</td>
</tr>
<tr>
<td>NCL1 – NIL1</td>
<td>-</td>
</tr>
<tr>
<td>NCL2 – NIL2</td>
<td>-</td>
</tr>
<tr>
<td>NI – NC</td>
<td>-</td>
</tr>
<tr>
<td>NIL0 – NCL0</td>
<td>RH: 44, -48, 43</td>
</tr>
<tr>
<td>NIL1 – NCL1</td>
<td>-</td>
</tr>
<tr>
<td>NIL2 – NCL2</td>
<td>RH: 48, -52, 43</td>
</tr>
</tbody>
</table>

**Main effect contrasts**

<table>
<thead>
<tr>
<th>hIPS activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Comparison Task – Identity Match Task</td>
</tr>
<tr>
<td>LH: -44, -44, 66</td>
</tr>
<tr>
<td>Identity Match Task – Comparison Task</td>
</tr>
<tr>
<td>-</td>
</tr>
</tbody>
</table>

Note. ROI had the form of a box extending 7mm, 5mm, and 6mm (LH), and 7mm, 7mm, and 5mm (RH) into x, y, and z dimension, respectively. The centre was located at Talairach coordinates (-44, -48, 47) for the LH and (41, -47, 48) for the RH. hIPS – horizontal aspects of the intraparietal sulcus; N – number; L – letter; I – identity match task; C – comparison task; L0 – lag 0; L1 – lag 1; L2 – lag 2; BH – both hemispheres; LH – left hemisphere; RH – right hemisphere
Interaction of WM Load and Stimulus Material

In order to study more closely the interaction of increasing WM load with different stimulus materials we compared directly those contrasts revealing increasing WM load for letters (i.e. [LIL2 - LIL1] and [LCL2-LCL1]) with those revealing WM demands using numbers as stimulus material (i.e. [NIL2 – NIL1] and [NCL2 – NCL1]). As we were particularly interested in semantic contributions of numbers used in WM-tasks, we first concentrate on contrasts that map number specific activation with increasing WM load: ([NCL2 – NCL1] – [LCL2 – LCL1]) and ([NIL2 – NIL1] – [LIL2 – LIL1]). We masked the contrasts inclusively with the contrasts revealing increasing WM load for numbers (i.e. [NCL2 – NCL1] and [NIL2 – NIL1], respectively) in order to avoid “artificial” activations due to double negative differences.

For comparison task we found increased activity due to presentation of numbers in the posterior middle temporal gyrus, bilaterally (BA 39), right superior temporal gyrus (BA 22), right inferior and left middle frontal gyrus (BA 45, and BA 9), cingulate gyrus (BAs 32, 31, 24), and bilateral superior parietal lobe (BA 7; all p < .05; uncorrected). Superior parietal activations resemble activations frequently found in studies where participants have to shift attention in space (e.g. Lepsien, Griffin, Devlin, & Nobre, 2005; Vandenberghe, Gitelman, Parrish, & Mesulam, 2001). Cingulate gyrus activity often is regarded as being due to increased task difficulty or error detection processes (Barch et al., 1997). No additional activity was observed in the hIPS. Identity match revealed activity in left precentral gyrus (BA 6), left middle frontal gyrus (BA 11), right superior temporal gyrus (BA 22), left middle temporal gyrus (BA 39) and insula (BA 13), as well as left lingual gyrus (BA 18) and right cerebellum (all p < .05, uncorrected). Neither brain regions frequently associated with processing of number magnitude nor WM-related areas were involved in this complex contrast.

While we did find additional parietal activation in interaction contrasts for the comparison task that might indicate some kind of semantic impact of numbers in WM tasks, we failed to find such an influence in the identity match task. Activation in the comparison task was not located in the hIPS proper but within adjacent parts of the parietal cortex that are supposed to contribute to orienting attention along the mental number line, i.e. the posterior superior parietal lobe (PSPL, Dehaene et al, 2003).

We computed the complementary interaction contrast of increasing WM load that is specific for letters ([(LIL2 – LIL1) – (NIL2 – NIL1)] and [(LCL2 – LCL1) – (NCL2 – NCL1)]). These were masked inclusively with letter specific contrasts [(LIL2 – LIL1) and (LCL2 – LCL1), respectively]: For the comparison task we found a network of activations comprising right premotor area (BA 4), bilateral cingulate gyrus (BA 31), left Insula (BA 13), left fusiform gyrus (BA 37), right middle (BA 8 & 10) and inferior frontal gyrus (BA 47), bilateral superior temporal gyrus (BA 22), right middle temporal gyrus (BA 39 & 37), left parahippocampal gyrus (BA 34), right postcentral gyrus (BA 5), left hemispheric fusiform gyrus (BA 19), as well as subgyral
activity in the claustrum. No ROI activity was observed. For identity match task we observed activations in bilateral middle frontal gyrus (BA 9), left lateraled inferior frontal gyrus (BA 46/47), bilateral middle frontal gyrus (BA 6 for LH and BA 10/46 for RH), right hemispheric premotor area (BA 6), right precentral gyrus (BA 4), left hemispheric parahippocampal gyrus, fusiform gyrus (BA 37) and middle temporal gyrus (BA 21), as well as right limbic lobe (uncus). Additionally, bilateral precuneus activity was observed (BA 7 and for RH: BA 19), and activity in right hemispheric lingual gyrus (BA 18). We observed left hemispheric hIPS (BA 40) activity for the interaction contrast in the identity match task.
5.4 Discussion

In this study we investigated the influence of different stimulus materials (letters vs. numbers) and tasks (identity match vs. comparison) in a verbal WM context (n-back task). Do averbal semantic characteristics of numbers influence information processing within verbal WM that is thought to rely on a phoneme-based, asemantic code? In order to increase the impact of semantic processing we introduced a variant of the n-back paradigm in which participants had to process items in terms of magnitude/alphabetical order (comparison task) instead of matching their identity. We tested Dehaene’s hypothesis of increased activity in the IPS when context explicitly requires accessing some sort of magnitude representation. The following paragraphs briefly summarize the results:

Behavioural data revealed that the tasks get more difficult with increasing WM load, i.e. RT and ER increase. Comparison is more difficult for letters than for numbers. For identity match few differences were observed between letters and numbers as stimulus material in a WM context. In the comparison task WM load interacts with stimulus material: While for low WM load numbers are responded to faster than letters, this advantage vanishes for high WM load.

Imaging data reveal a pattern of activations that is highly consistent with results obtained in former WM studies: Increasing WM load activates DLPFC and PC (see Figure 2). For the number specific contrast (NL2 – NL1), additional activity was observed in the anterior cingulate gyrus. Activity extended into supplementary motor areas (SMA), which might be a correlate of the larger RT difference between lag 2 and lag 1 for numbers and letters in the comparison task that lead to longer response preparation. Comparing the task specific contrasts with each other (i.e. NIL2 – NIL1 & NCL2 – NCL1) has lead us to suggest that this activity is most likely due to the identity match task. This in turn implies that the comparison task is easier to perform than matching the identity of numbers.

Stimulus specific influences can be divided into number and letter specific brain activity: No additional hIPS activity was observed contrasting numbers against letters (N – L). Neither did numbers induce additional activity in the hIPS when we analyzed each task separately (NI – LI; NC – LC). However, separately analyzing the different task X lag conditions reveals that numbers indeed add additional activity to the hIPS in verbal WM tasks: This additional effect was present in contrast (NIL1 - LIL1). For letters neither the main 6Recently, SMA and AC activity has been implicated in both conflict monitoring - i.e. they show greater activity when conflicting response alternatives have to be resolved (Braver, Barch, Gray, Molfese, & Snyder, 2001) - and error monitoring (Kiehl, Liddle, & Hopfinger, 2000) processes. This makes sense given the high complexity and difficulty of the 2-back condition as compared to the 1-back condition.
effect (L – N) nor did the task specific contrast for identity match task (LI – NI) reveal ROI activity. However, bilateral hIPS activity was observed in contrast LC – NC. When separately analyzing each combination, letters induced additional bilateral activity in the hIPS in two conditions (i.e. LCL0 – NCL0, and LCL2 – NCL2).

According to Dehaene and colleagues (2003), explicitly referring to numerical magnitude should induce additional impact on the magnitude representation which is thought to be located in the hIPS. This postulate was extended to the alphabetic sequence dimension, which may be also associated with hIPS activity (see introduction). When testing this task specific modulation of hIPS activity we found a pattern of results that is not completely consistent with this assumption: While it holds for letters, i.e. LC – LI reveals hIPS activity, this is not the case for numbers: We did not observe hIPS activity in contrast NC – NI. Keeping WM load and stimulus type constant, corresponding contrasts revealed hIPS activity in letter specific conditions (LCL1 – LIL1, LCL2 – LIL2), while for number specific conditions no activity was observed in the hIPS. Indeed, for numbers a reversed pattern of results was observed: Contrasting NI against NC (NI – NC) induced additional hIPS activity. In sum, our results seem to be at odds with Dehaene’s hypothesis in the context of a WM task.

In order to disentangle contributions of stimulus material and WM load we computed interaction contrasts: The interaction between WM load and stimulus material for the comparison task ([NCL2 – NCL1] - [LCL2 – LCL1]) revealed activity in superior PC for numbers. The interaction contrast for letters in identity match task ([LIL2 – LIL1] – [NIL2 – NIL1]) revealed activity in right parietal cortex (BA 7/40) including the hIPS.
6 General Discussion

The General Discussion will focus on three major issues:

1. The nature and properties of the mental representation of two-digit numbers in magnitude comparison tasks.
2. The neural implementation of two-digit number comparison.
3. The impact of numbers in the assessment of verbal working memory.

As far as the first two issues are concerned, the results of Experiments 1 to 3 of Study 1 will be briefly summarized before an extension of the theoretical framework of two-digit number comparison provided by Nuerk & Willmes (2005) will be provided. Based on the results of Study 2 and Study 3 the question will be discussed how some of the processes proposed may be implemented in the brain. A functional segregation of the hIPS will be proposed separating anterior medial parts of the hIPS from posterior parts.

The results of Study 4 will serve as a basis to discuss how verbal working memory may be influenced by numerical semantics.

This thesis will finish by pointing to possible future experiments that might help to further clarify the cognitive architecture of the topics raised.
6.1 On the Structure of the Numerical Magnitude Representation and Two-Digit Number Magnitude Comparison

6.1.1 The Structure of the Mental Representation of Two-Digit Number Magnitude

In the following, the structure of the mental representation of two-digit numbers will be elaborated on. Furthermore, an extension of the theoretical framework of two-digit number magnitude comparison proposed by Nuerk and Willmes (2005) will be described. First, a brief summary of the main findings of Study 1 will be provided before discussing these results on the background of the results from other studies concerning two-digit number processing.

Study 1 yielded the following main results:

1. Unit-related effects are strongly modulated by SOA:
   a. In Experiment 1 and Experiment 3, positive SOAs produced a stronger impact of unit distance on the overall magnitude comparison process than negative SOAs. In Experiment 2, the interaction of SOA and units pointed to the opposite direction, now yielding a larger impact of unit in negative SOAs. This discrepancy will be dealt with later on.
   b. The SOA range strongly determines the impact of the units. The SOA range chosen by Dehaene was suboptimal since we observed the strongest impact of unit at SOAs of +50 and +100 in Experiments 1 and 2.

   These unit-related effects clearly speak in favour of the so-called interference model, discarded by Dehaene and colleagues on basis of their results. The interference model resembles the hybrid-model of Nuerk and Willmes in that it assumes separate representations of units and decades. Most importantly, the results speak against a holistic number representation but support the notion of separate representations for units and decades.

2. Beyond unit-unit and decade-decade magnitude comparisons, the regression analyses in Experiment 3 revealed that even the intra-number digit distances, i.e. the numerical magnitude codes of the constituting digits significantly influence the overall comparison process. Therefore, the results of Experiment 3 are in line with the results of Wood and colleagues (2005). This strongly supports the assumption of an automatic access of digits to the mental magnitude representation. Moreover, it implies that the magnitude representations and the magnitude comparisons the participants engage in do not seem to be under conscious control of the participants.

3. The stimulus material significantly influences the unit-related effect:
a. Using a fixed standard of e.g. 65 allows for a maximal unit distance of four. This is close to the range of the so-called small unit distance in Experiments 1 to 3. Compatibility effect was smaller for this unit distance range than for large unit distances. This might explain the null-effect observed by Dehaene and colleagues (1990).

b. The relevance of the unit digits has a major impact on the size of the compatibility effect. This factor seems to be subject to influences of either internal, subjective salience judgements of the participants or external changes.

   i. Internal salience judgements (top-down) are based on the degree to which each digit is informative with regard to the decision that has to be made.

   ii. External factors (bottom-up) like e.g. the on-screen position of the units and decades or the mask used also influence the salience of the unit digits.

Taken together these results suggest that a two-digit magnitude comparison is far from being an automatic process which is not due to internal or external influences. Assuming that overall magnitude, decade magnitude, and unit magnitude contribute to the comparison process, these results suggest a highly flexible amount of contribution of the respective magnitude representations. Therefore, the magnitude comparison process of two-digit numbers appears to be both stimulus-driven and prone to attentional/strategic influences.

The structure of the mental representation of two-digit numbers has been under debate for quite a while. On the one hand there was the notion of a single holistic magnitude representation of two-digit numbers, most prominently represented by Dehaene and colleagues (e.g. Dehaene et al., 1990, 1993, 1998). On the other hand there was the proposal of a totally decomposed number representation by McCloskey (1992). However, recent results suggest the existence of both a holistic representation of two-digit number magnitude and decomposed magnitude codes of two-digit numbers (cf. Nuerk & Willmes, 2005). The results of Study 1 add evidence to the existence of decomposed representations of unit and decade magnitude (see Nuerk & Willmes). Experiments 1 to 3 were conducted to test the prediction of the holistic approach against decomposed magnitude representation. A reliable influence of units was observed in all three experiments. This influence cannot be explained by assuming only a single access to one holistic magnitude representation. Rather, one needs to assume the existence of additional representations for units and decades. This is in accordance with the results from Nuerk and colleagues who have used the unit-decade
compatibility effect in various experimental paradigms and consistently found the units to influence the process of magnitude decision (Nuerk, Weger et al., 2001, 2002, 2003, 2004). Moreover, these results are partially in line with the results of Verguts and De Moor (2005) who found the magnitude comparison of two-digit numbers to be mainly influenced by decomposed magnitude representations. More specifically, the authors argue that the magnitude comparison of two two-digit numbers is accomplished by a “recycling” of the decomposed digit representations (p. 199; Verguts & De Moor, 2005). The overall magnitude representation is postulated to be too fuzzy to be used to this end. This is argued to be due to the infrequent use of two-digit numbers larger than 15 in every-day life. Verguts and De Moor base their claim of a magnitude comparison process totally relying on decomposed magnitude codes on the absence of a distance effect in between-decade trials which were restricted to a decade distance of one. If the overall magnitude influenced the comparison process, it is argued, one would expect a regular distance effect in this condition, too. However, the authors did not take into account the compatibility of the number pairs. That is, the way of stimulus construction produced a set of number pairs which were matched for overall distance between within-decade and between-decade trials. However, for between-decade trials, the unit-decade incompatibility increased with increasing overall distance. For example, a number pair like 48_54 is matched in terms of overall distance with a pair like e.g. 23_29 (6 in both cases). However, the latter number pair is compatible while the first one is not. While for within-decade number pairs these two measures do not differ, for between-decade trials they influence responses in different directions (see Table 15 for details). This presumably has caused the observed null-effect for between-decade trials. Note also, that the situation from the participants view was comparable to Experiment 2 of Study 1 since it was unclear in advance, which digit would be relevant for the decision. In 50% of the trials, participants had to base their decision on the comparison of the units and in 50% of the cases on the decade digit compassion. In Experiment 2 it was shown that such a proportion of within and between-decade trials maximizes the influence of the units. Moreover, the decade distance always was set to a maximum of 1. Again, the results of Experiments 1 to 3 show that small decade distance trials favour the appearance of unit-decade compatibility effects. Therefore, the results of Verguts and De Moor are not appropriate to discard the presence and influence of an overall magnitude representation beyond the decomposed representations.
Table 15: Stimulus properties of the stimulus set of Verguts & De Moor (no filler trials). Note that unit-decade compatibility and overall distance point to different directions for between decade trials

<table>
<thead>
<tr>
<th>Decade distance</th>
<th>Overall Distance</th>
<th>Mean overall distance</th>
<th>Mean unit distance</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Small</td>
<td>2.33</td>
<td>2.33</td>
</tr>
<tr>
<td>0</td>
<td>Large</td>
<td>6.14</td>
<td>6.14</td>
</tr>
<tr>
<td>1</td>
<td>Small</td>
<td>3.00</td>
<td>-7.00</td>
</tr>
<tr>
<td>1</td>
<td>Large</td>
<td>6.69</td>
<td>-3.31</td>
</tr>
</tbody>
</table>

What about the reported null-effect in Experiment 4 of the Dehaene et al. (1990) study? Instead of supporting the notion of an exclusively holistic magnitude representation, the contradictory null-effect finding of Dehaene and colleagues may have been due to the (i) narrow range of possible unit distance and (ii) the SOAs used (-50, 0, +50). First, for number pairs with a small unit distance (i) which were well comparable to the stimuli of Dehaene et al., we failed to find SOA modulations of unit-based compatibility effects, thus essentially replicating their results. This seems to suggest that the analogue interpretation of Dehaene and colleagues may only hold for specific stimulus set properties. Second, we observed somewhat weaker SOA modulations when only the SOAs [-50, 0, 50] of Dehaene et al. were used than when a wider range was employed (see Experiments 1 & 3). For these reasons, we conclude that the absence of an SOA modulation of unit-based effects observed by Dehaene et al. might not be conclusive for rejecting decomposed processing of tens and units (cf. also McCloskey, 1992).

In sum, the model explaining the present data and the data from the literature best is the hybrid model of Nuerk and Willmes (2005). Two-digit numbers seem to be represented in a hybrid fashion, i.e. holistically and decomposed.
6.1.2 The Magnitude Comparison of Two-Digit Numbers

Beyond the question of the nature of the mental representation of two-digit number magnitude the data serve to further specify some features of the mental mechanisms involved in two-digit magnitude comparison. Especially the results of the regression analyses of Experiment 3 imply that participants engage in all kind of magnitude comparisons based on different codes: Beyond comparing overall magnitude, decade magnitude and unit magnitude of both numbers with each other, participants compare the unit and decade digits of one number with each other and with the digits of the second number. The results are consistent with the study of Wood and colleagues (2005). Wood and colleagues have varied the SOA of units and decades in a magnitude comparison task in an asymmetric way, i.e. the unit digit of one number appeared together with the decade digit of the second number. Using this experimental setting, Wood and coworkers obtained second order compatibility effects, too. Therefore, it appears that participants engage in numerical magnitude comparisons as soon as two digits appear on screen. This process seems to be highly automatic, since in some cases this comparison process was at odds with the task at hand and did not yield a benefit for the relevant decision but hampered the decision process. The second order congruency effect obtained in the Wood et al. (2005) study and in Experiment 3 of Study 1 provides a good example of a detrimental comparison. It indicates that participants could not willingly refrain from comparing the two digits with each other which slowed down the decision in some cases. Even when participants tried to concentrate on the decade digits only (as they reported after Experiment 1) the unit digits did have some impact on the comparison process. Taken together this implies that the numerical magnitude of the constituting digits in a two-digit magnitude comparison task is not only automatically activated in a decomposed fashion. It also implies that the activated magnitude representations are compared to each other, and that this comparison process is not happening in a column-wise fashion only, but also diagonally and horizontally. This in turn might be interpreted as indicating a digit-based comparison process which does not take into account the digits’ position. That is, if the digits’ position would be taken into account at this stage of information processing, participants would either not engage in a comparison process at all or at least the outcome would hardly be influencing the overall comparison process. In the above mentioned example from the Wood et al. (2005) study, comparing the 5 from 54 against the 7 from 27 can influence the response times only when participants do not take into account its position and the value due to its position. Otherwise it would be hard to imagine how comparisons like 50 _ 7 with a very high overall distance (here: 47) could slow down the overall comparison. This might be taken as evidence for a relative larger importance of digits’ magnitude representation in the process. The coding of decade or unit
magnitude might therefore be accomplished by simply adding some kind of ‘flag’ to each single, indicating its power of ten. If so, the overall magnitude representation might be computed by an internal addition of both flagged digits. This is in line with the proposal of Hubbard and colleagues who speak of mental arithmetic in terms of spatial movements along the mental number line (Hubbard et al., 2005). Moreover, this view is consistent with a logical argument. When processing two-digit numbers, the first step inevitably is the identification of the constituting digits. Therefore, the digits’ magnitude might be the first magnitude representation that is accessed. One might assume that beyond the activation of the respective numerical magnitudes of the “integrated” digits - i.e. the digit has already been assigned a power of ten - the single digits in parallel activate the respective unit magnitude.

The magnitude comparison process is subject to two kinds of processes both liable to change the relative contribution of the assumed comparison processes (see below) to the response stage, presumably to the stage of response selection. These processes can either be classified as working in a top-down or in a bottom-up fashion.

The most prominent top-down process influencing the magnitude comparison process in Study 1 was the strategy to focus in the decade digits only in Experiment 1. Since the decade digits were informative in 100% of the trials, this strategy was quite efficient in terms of minimizing the effort needed to complete the task. This becomes evident in the small compatibility effect which was only present in large unit distance trials. However, when the decade comparison and the unit comparison are both decisive in 50% of the two-digit comparisons (see Experiment 2), unit-based effects for the identical stimulus subset did not only reappear, but were larger than in any previous study. By slightly jittering the horizontal position of the (relevant) digits unit-decade compatibility effects were observed, which numerically are intermediate between Experiment 1 and Experiment 3. We suggest that participants focus their attention on the location of the decade digits when they are 100% relevant and when the perceptual settings allow such a strategy. This attentional focus on the 100% relevant decades diminishes unit-based effects. When decades and units are equally decisive (Experiment 2) or it is not clear what power of ten has to be assigned to the pair of digits appearing first (Experiment 3), this attentional strategy is useless (see below). Hence, unit-based effects reappear. These data imply that a stimulus-induced strategy can influence number processing effects even in task as simple as two-digit magnitude comparison.

Focusing on the decade digits minimizes the salience of the unit digits, and thus can be regarded as a top-down modulation of the comparison process. Beyond this, bottom-up processes can change the units’ salience, too. That is, in Experiment 2 and Experiment 3, we changed the unit digits’ salience in two ways: Either we introduced number pairs that could be distinguished based upon the unit information only, or the on-screen position of the units was changed slightly from trial to trial. As noted above, under these circumstances, the
compatibility effect reappeared. The units gained salience which bolstered their impact on the magnitude comparison process.

How can the apparently contradictory influence of SOA on the compatibility effect be reconciled? In Experiment 1 and Experiment 3 the compatibility effect increased with increasing SOA. In Experiment 2 this influence was reversed, now yielding a decreasing compatibility effect with increasing SOA. For Experiment 1 and 3 the explanation of the SOA X compatibility effect is simple: Since participants knew in advance that the digits appearing right of the decade digits (in Experiment 3 this judgement was based on the spatial relations of the respective digits) were irrelevant for the overall decision they inhibited these digits. This inhibition seemed to be triggered by the stimulus appearing first and influenced by the a priori knowledge about the stimulus set containing only between-decade trials: It seemed to start immediately after the decade digits were presented, thus leading to a diminished unit influence of units in negative SOAs. In trials with positive SOAs the inhibition started after the presentation of the first pair of digits, too. However, in this case the numerical meaning of the unit digits became activated automatically and influenced the overall decision process more than in the reference condition (SOA = 0) or with negative SOAs. This lends further support to the assumption of numbers automatically accessing numerical magnitude upon presentation. Interestingly, this process was modulated by the amount of temporal asynchrony of decades and units even within the positive SOA only. The strongest impact was observed with short SOAs (50 & 100 ms). When the SOA was large (e.g. 400 ms) the influence of the units was diminished again. This is presumably due to the fact that at this point of time the magnitude comparison of both digits was finished and could thus be well inhibited. In Experiment 2, participants could not inhibit unit digits based only on their temporal or spatial position in the trial. In this Experiment the unit digits were relevant in 50% of the trials. Therefore, participants seemed to process all digit information provided without an a priori bias as in Experiments 1 and 3. In this situation, the pair of digits appearing second seemed to attract more attention than the digits appearing first, similar to the results of Wood and coworkers (2005). This attentional shift is known from the domain of visual attention and apparent movement. In contrast to Experiments 1 and 3, it was not mitigated or modulated by any strategic bias towards one side of the object/number. This reversed the interaction of SOA and compatibility with respect to Experiment 1 and Experiment 3. Again, a combination of top-down (strategical/attentional) and bottom-up (stimulus based) factors influenced the comparison process.

Taken together, the results form Experiments 1 to 3 suggest that in a two-digit number magnitude comparison task neither only the overall magnitude of the two numbers are compared to each other nor the constituting digits in terms of their decomposed magnitude are compared to each other (i.e. in a number pair like 42_57: 40_50 and 2_7). Rather, all
kinds of possible comparisons seem to be carried out, irrespective of whether they are useful for the task at hand or not. These automatic comparison processes are even apt to override strategic and attentional biases of the participants, as demonstrated in Experiment 1. On a more general level, our data also imply that both top-down and bottom-up mechanisms influence performance in a task as simple as magnitude comparison. Putatively, this is done by changing the relative weights with which the respective magnitude comparisons contribute to the accumulating response process (see below).

The exact mechanisms will be described in the next section.
6.1.3 Extended Framework of Two-Digit Number Magnitude Comparison

In this part of this thesis the framework of two-digit number magnitude comparison proposed by Nuerk and Willmes (2005) will be extended. In detail, two modifications are suggested:

1. Beyond the comparison of overall number magnitude, decade magnitude and unit magnitude of both numbers (see Nuerk & Willmes, 2005), a magnitude comparison of each possible pair of constituting digits is proposed. This process is performed on basis of the respective digit magnitude (0 to 9).

2. The amount of activation each single comparison process adds to the response stage depends on the assigned relevance of the particular comparison in the given experimental situation. This is due to strategic/attentional changes.

In a second step the postulated processing steps will be related to their neural correlates. That is, which brain areas are associated with the processing of unit magnitude, decade magnitude and overall magnitude? If unit-decade compatibility activates a distinct cortical area in the anterior IPS, do we need to consider additional areas?

The model of Nuerk and Willmes suggests the existence of three magnitude representations in situations when we perceive a two-digit number: The overall (analogue) magnitude representation of the number, the decade magnitude representation and the unit magnitude representation. In a two-digit magnitude comparison task, these different representations are postulated to be compared to each other. In detail, Nuerk and Willmes assume that the overall magnitude representations of both numbers are compared to each other, the decade magnitude representations are compared to each other as well as the unit magnitude representations (see Nuerk & Willmes, 2005). In incompatible number pairs the unit comparison leads to a result diverging from the results of the other two comparisons. Since all comparison processes are assumed to spread their activation to the output level (i.e. response selection, response preparation or response execution) the unit comparison has negative contribution to the correct response. This leads to a decelerated accumulation of activation for the correct response. This in turn postpones the point of time when a critical difference of activation (threshold) is exceeded. Thus, incompatible trials are responded to more slowly than compatible.

However, the story seems to be more complex. Experiment 3 of Study 1 shows that in some situations participants tend to compare the digits of one number to each other (cf. Wood et al., 2005). The congruency-coded (i.e. is the result congruent with the overall comparison?) distance of this digit comparison became a significant predictor in a regression analysis computed to reveal significant predictor of response latencies. This leads to the
proposal that each digit presented in the stimulus pair on screen activates the respective unit magnitude representation. These digits are compared to each other in turn. The comparisons are not restricted to decade-decade comparisons of both numbers or decade-unit comparison within one number. Wood et al. (2005) showed that even the decade digit of the first number (62 → 6) is compared to the unit digit of the second number (47 → 7; resulting in a digit comparison of 6 versus 7). This process seems to be automatic, since it cannot be overruled by strategy completely (see Experiment 1 of Study 1). However, the results of the different comparison processes are weighted differentially. This means, that the contribution of the single comparisons to the response stage is not a fixed value. It is subject to strategic and attentional changes that modulate the relative salience of the respective comparison in accordance with (i) stimulus set properties (see Experiment 1 & Experiment 2 of Study 1), and (ii) procedural settings of the experiment (see Experiment 1 and Experiment 3 of Study 1).

One might argue that it is not necessary to assume an additional process of decade digit x unit digit comparison which calls for additional magnitude representations. The comparison process might as well operate on the magnitude codes already postulated by Nuerk & Willmes (2005). However, it is hard to imagine that a magnitude comparison like e.g. 60_2 or 40_7 in a number pair of 62_47 would enter regression analysis as a significant predictor given the overall distance of 58 (= 60 – 2) or 33 (= 40 – 7).

The extended model of Nuerk and Willmes is shown in Figure 27. When presented with a number pair like e.g. 47_62, the numbers are perceived as two objects, containing two elements each, and as a set of four different digits. The overall two-digit numbers activate the overall magnitude representation. The decades activate the decade magnitude representation. The units and the decade digits activate the unit/digit magnitude representation. All these mentally represented numbers are then parsed to the magnitude comparison level. At this stage of information processing the respective representations are compared to each other as shown in Figure 27. Each comparison process activates both response alternatives. Congruent responses contribute via excitatory connections (black), incongruent via inhibitory connections (grey). The strength of activation is determined by the respective weight of the connection. These weights are influenced by overall strategic/attentional processes which in turn result from stimulus set attributes and experimental settings. In the model two different weights for decade magnitude/overall magnitude and unit/digit magnitude are depicted. The different unit/digit magnitude comparisons are not thought to have identical weights. Rather, it is assumed that the weights are determined in a flexible way. The actual weight of the respective comparison depends on its salience. This again is modulated by the above mentioned factors, among them bottom-up/stimulus-driven factors as well as top-down strategic considerations. One major heuristic
to determine a given digits’ relevance may be taking into account its position within the number. However, since the magnitude representation of a given digit is activated automatically, the weight cannot be set to zero. Experimental settings can be used to modulate the weights, although the particular comparison may not at all be useful for the required decision. For example, in Experiment 3 of Study 1, a comparison like 6_2 for a number pair like 62_47 is not helpful for the decision which of both numbers is numerically larger. Nevertheless it significantly contributed to response latency as indicated by the performed regression analyses. This particular comparison was even diminished in saliency by the asynchronous presentation, i.e., by the experimental setting.

This model can easily be extended to multi-digit numbers. In multi-digit numbers it is assumed that the decomposed magnitude representations gain importance since the overall magnitude representation becomes increasingly fuzzy with an increasing number of constituting digits (cf. Poltrock & Schwartz, 1984; Verguts & De Moor, 2005). This should increase the impact of determining response weights of particular digit comparisons in accordance with the digits’ positions in the given numbers.
Figure 27: Extended framework of Nuerk & Willmes (2005) for two-digit number magnitude comparison. Connections from single magnitude comparisons to output level can either be congruent (black) or incongruent (grey) with the decision.
6.2 Neural Implementation of Two-Digit Number Magnitude Comparison

In Study 2 we investigated the neural correlates of two-digit magnitude processing. We were interested in the cortical areas associated with (i) the processing of numerical magnitude and the question whether the IPS is organized in a numerotopic way and (ii) the integration processes of unit and decade digits into an integrated number. We have extended the stimulus set used by Wood, Nuerk and colleagues (2006) by including trials from the same decade (within-decade trials). This offered the opportunity to investigate the neural correlates of the semantic interference which is induced by the unit digits without confounding numerical magnitude information. Moreover, this has been shown to increase the compatibility effect (i.e. the amount of semantic interference) by increasing the salience of the unit digits (see Study 1).

There were two main findings from Study 2:

1. No evidence was observed which would allow assuming a numerotopic organization of the neural correlates for number processing in the intraparietal sulcus. That is, neither unit distance in within decade trials nor decade distance or unit distance in between decade trials have been found to activate specific and unique areas in the IPS. In contrast, we observed a large network of areas along the IPS which were commonly activated by numerical distance in either stimulus class. We found this network to be more pronounced in the left hemisphere. This hemispheric asymmetry was due to the fact that the left anterior bank of the IPS was activated by both predictors in the multiple regression analysis, whereas only posterior aspects were active in the right hemisphere. The conjunction analysis revealed less activation than the multiple regression approach. Moreover, the conjunction analysis revealed a left-hemispheric cluster of activation in the posterior IPS, and no such activation on the contralateral site. Taken together, this implies that bilateral posterior aspects of the IPS are associated with processing of numerical distance, with the left hemisphere being involved more extensively. Left-hemispheric anterior aspects of the IPS seem to be involved in the processing of numerical distance information less consistently.

2. We observed a left-lateralized activation in the anterior IPS which was associated with unit-decade (in)compatibility. By subtracting unit-digit related activation, we were able to show that this cluster of neurons might be involved in processing semantic interference in a more general meaning, i.e. separated from numerical distance information. This area was left-lateralized, as could be demonstrated by contrasting it to the contralateral homologue area. The left-hemispheric activation remained significant. This area in the left IPS was specific to semantic interference. We showed that the activated regions in the conjunction analysis of decade and unit distance were located in the posterior aspects of the
IPS (lateral to the activation of semantic interference). The activation of unit-decade compatibility was located on the medial bank of the anterior IPS, however. This region was not active in any contrast involving numerical distance information.

Study 3 was set up to investigate the functional necessity of the area around the IPS for two-digit number processing. The stimulus set used allowed investigating two aspects of this complex process (see page 144) at a time. The distance effect can be regarded as a marker indicating access to the mental magnitude representation (mental number line). The compatibility effect indicates a semantic conflict between unit and decade magnitude which might reflect an impaired integration process of both streams of information. If the activations observed for numerical cognition (see e.g. Study 2) are functionally relevant for the execution of a comparison task, inducing a virtual lesion by rTMS should reduce signal to noise ratio in that process. This in turn should result in an increased distance effect (cf. Delazer et al., 2006). The same rationale holds for the compatibility effect: If the results of Study 2 are valid, the left hIPS is involved in the resolution of the semantic conflict induced by incompatible decade-unit information. Therefore, the compatibility effect should increase after inducing a virtual lesion in that area.

The results seem to be consistent with the assumed role of the hIPS. Both distance effect and compatibility effect were modulated by rTMS over the left IPS. In contrast, stimulation over vertex did not change the effects under scrutiny here. The pattern of results was more complex, however. The impact of TMS on the cognitive effects was modulated by gender. Keeping two assumptions in mind helps to interpret the results:

1. The amount of transcallosal transfer differs between both genders. The corpus callosum in female participants tends to be larger than in male participants (see Steinmetz et al., 1995).

2. Both hemispheres differ in terms of processing style: While the left hemisphere is more concerned with an analytic style of information processing, the right hemisphere is thought to favour holistic aspects of a given stimulus. In number processing, this may address decomposed processing of two-digit number magnitude as opposed to analogue/holistic processing.

Therefore, the increased compatibility effect in female participants is consistent with a larger impact of rTMS on both hemispheres due to a larger amount of transcallosal transfer as compared to male participants. This leads to an increased compatibility and (numerically) increased distance effect. In male participants on the other hand, the left hemisphere was affected more than the right. Since both hemispheres are capable of numerical magnitude comparisons (see Study 2), the right hemisphere may have had a processing advantage in this situation. Decomposed processing has repeatedly been found to be particularly difficult
when the magnitude comparison is incompatible and when the distance between the two numbers is small (Nuerk, Weger et al., 2001, 2002; Nuerk & Willmes, 2005). In these conditions, decomposed processing produces much interference. In contrast, holistic processing does not produce any such interference in incompatible trials. If male participants process two-digit numbers to a greater extent by holistic processing, they should benefit (relatively) most in exactly those conditions in which decomposed processing is detrimental. Such a condition is the small-decade distance /incompatibility condition. In that specific condition, holistic processing should lead to greater improvement than in any other condition (in particular compared to any large decade distance condition). In this way, holistic processing would decrease the distance effect, however, only for incompatible trials for which decomposed processing is detrimental. This is exactly what has been observed in the data: rTMS in males led to particularly faster response latencies in incompatible trials with small decade distances.

Taken together, the results of Study 3 corroborate earlier findings that the hIPS plays a major role in processing numerical magnitude information. Moreover, they suggest a major contribution of the left parietal cortex to the correct integration of different streams of numerical and spatial information in this comparison process as indicated by the modulated compatibility effect.

Based on the findings from Study 2 and Study 3, the existence of two separate neural circuits within the parietal cortex is suggested. One neural circuit is involved in the representation of the numerical magnitude information. This functional network comprises bilateral areas of the posterior part of the IPS, lateral to the interference activation. The second functional system is involved in (i) either the representation of concurring response alternatives in situations with (semantic) conflict or (ii) the resolution of these semantic conflicts. This system seems to be left-lateralized. Moreover, it is implemented in neural assemblies that are located on the medial wall of the anterior part of the IPS. Beyond parietal cortex, left prefrontal cortex seems to be involved in this network.

These assumptions can be related to the extended framework of two-digit number magnitude comparison (see above).

First, it is suggested that the postulated mental representation of both decomposed and holistic numerical magnitude is located in the neural network described first. That is, bilateral aspects of the hIPS seem to contribute to the mental representation of numerical magnitude information. This is in line with the functional-anatomical model of Dehaene and Cohen (1995), which assumes a bilateral representation of numerical magnitude information. Therefore, this suggestion extends the repeatedly observed bilateral activation of the hIPS in tasks that rely on the processing of numerical magnitude information of one-digit numbers
A bilateral representation of one-digit number magnitude has also been proposed on the basis of behavioural findings in visual half-field tasks (e.g. Ratinckx & Brysbaert, 2002). Moreover, this is consistent with the ATOM theory by Walsh (2003), who suggests that numerical, temporal and spatial magnitude codes rely on common neural metrics, being located in the hIPS, bilaterally. Based upon the results of Study 3, one may assume that the left hemispheric parts of the IPS are more important for representing the decomposed numerical magnitude information whereas the holistic magnitude information might predominantly be represented in the right hemisphere. This view is consistent with recent results from a TMS study (Andres et al., 2005). Here, the authors argue that the LH is capable of precise numerical judgements while the RH is restricted to approximate judgements of numerical magnitude. This left-hemispheric specialization is hypothesized to result from a link between (finger) counting strategies and language functions, which are thought to be left-lateralized. Note that in the study of Andres and coworkers, TMS over the left PC had the strongest differential impact on the numerical judgements: After left-hemispheric stimulation the RT in trials with a small numerical distance were slowed down when compared to RH or sham stimulation. This led to an increased distance effect. When computing the respective estimated effect sizes (Kirk, 1995) from the reported data, the distance effect after LH stimulation (d = .50) was larger than after stimulation of the RH (d = .32), both hemispheres (d = .26) or sham stimulation (d = .27). In contrast, bilateral stimulation affected both small and large numerical distances. This did not increase the distance effect but hampered both hemispheres alike. This TMS finding is also in line with results from patient studies. Damage to the left parietal cortex has frequently been reported to result in severe impairments of numerical abilities such as calculation (Mayer et al., 2003), magnitude approximation (Lemer, Dehaene, Spelke, & Cohen, 2003) or transcoding of two-digit numbers (Blanken, Dorn, & Sinn, 1997; Proios, Weniger, & Willmes, 2002).

Note that previous research has revealed a link between visuo-spatial properties of the perceptual display of numbers in experimental settings and the assumed mental representation of numerical magnitude (e.g. Ratinckx & Brysbaert, 2002; Brysbaert, 1995). However, this is different from the representational differentiation proposed here: The proposed hemispheric differentiation is not based on congruency between external and internal representations. Rather, it is assumed that the neural implementation of different internal numerical magnitude representations (holistic vs. decomposed) relies on the two hemispheres to a different degree.

Second, it is suggested that the interaction of strategic/attentional processes with the relative contribution of the separate magnitude comparison results (i.e. unit – unit, decade –
decade, overall – overall magnitude comparisons) has its neuronal correlate in the interplay of left anterior parietal and left prefrontal structures. Here, the postulated top-down and bottom-up processes influence the choice of the correct response alternative by flexibly changing the relative weights of the magnitude comparisons. Therefore, the observed left parietal cortex activation in the medial bank of the IPS might be due to the process of response selection which has previously been shown to activate left anterior parietal areas. Attentional/strategic biases presumably have their neural correlate in the left prefrontal cortex. Prefrontal cortex has repeatedly been associated with top-down control mechanisms of behaviour in various tasks like working memory tasks (Smith & Jonides, 1999), or Stroop paradigms (e.g. Milham et al., 2001; MacDonald et al., 2000). In the context of the latter class of tasks, the role of the PFC is clearly distinguished from the role of other frontal regions like for instance the ACC. That is, the PFC (BA 9) is supposed to be engaged in the attentional control of task-appropriate behaviour. Interestingly, the left DLPFC is thought to aid in non-response aspects of selection (Liu et al., in press). In contrast, the ACC is thought to take over evaluative functions which indicate when more control is needed (MacDonald et al., 2000). This is consistent with the observation that the ACC is often reported to be involved in error monitoring functions. Note however, that in the present study the centre of activation in the middle frontal gyrus was located slightly posterior to BA 9. Brodmann area 8 has been reported to be involved in the temporal organization of task demands in dual task paradigms (Szameitat, et al., in press). Other researchers associate activity in a network comprising left prefrontal and inferior parietal cortex with the coordinated manipulation of simultaneously presented information (Collette et al., 2005). Therefore, the observed activation might as well reflect the coordinated manipulation of the different and partially contradicting magnitude comparisons in order to choose the appropriate response alternative. Rather than reflecting processes related to response selection, the left medial frontal cortex has been argued to be involved in selecting the relevant task context whenever the situation contains conflicting information (Brass & von Cramon, 2004). This particular region is located in the inferior frontal gyrus, however. That is, despite the overall distance between these two regions (left inferior frontal gyrus and left medial frontal gyrus) might not be too large, functionally they are probably well separated. The same authors observed activation in left anterior IPS, very close to the cluster of activity found in Study 2 (see Figure 16). They interpreted as being related to motor attention rather than visual selection. This is in line with the interpretation of the current cluster in the left medial wall of the IPS to be related to the interaction of diverging response tendencies.
6.3 The Impact of Numbers in the Assessment of Verbal Working Memory

The following section deals with the question whether numbers are well suited to serve as verbal (asemantic) stimulus material in the assessment of vWM.

6.3.1 Semantic Influence of Numbers in vWM

Based on the results reported we suggest that in WM tasks the hIPS activity is modulated by interaction of task demands and the stimulus material employed: Numbers induce activity that may be related to processing of magnitude information. Imaging data allow for this interpretation even though no behavioural effect is evident (e.g. hIPS activation in contrast Number Identity task Lag 1 – Letter Identity task Lag 1; NIL1 – LIL1). A specific influence of numbers on WM performance seems to depend (i) on the task executed and (ii) the WM load. Behavioural data revealed number related advantages only in the comparison task with low WM load. This advantage vanished, however, with increased WM load, i.e. no significant difference was observed between letters and numbers in lag 2 (Letter Comparison task Lag 2 vs. Number Comparison task Lag 2; LCL2 – NCL2). Taken together, there was little evidence for a semantic influence of stimulus material on performance in verbal WM tasks. Only when the task explicitly addresses some sort of comparison process, participants benefit from the fact that numerical meaning is accessed highly automatically for numbers while for letters a comparable process is more effortful (i.e. referring to the alphabet sequence takes longer and is more error prone). Using numbers instead of letters in an n-back task does not consistently induce additional hIPS activity that is indicative of numerical processing. At least two possibilities may account for this pattern of results: First, there was no hIPS activity that can be related to processing numerical magnitude at all. This is rather unlikely since (i) numerical magnitude related hIPS activity has been shown in a large number of fMRI studies (e.g. Dehaene et al., 2003; Fias et al, 2003; Naccache & Dehaene, 2001). (ii) In line with this general argument in the current study the PC including the hIPS was active in all conditions including numerical stimuli. (iii) It has been shown repeatedly that numerical meaning is activated irrespective of the context even in situations when participants actively try to concentrate on non-numerical stimulus features of numerical stimuli (e.g. Fias, 2001; Schwarz & Ischebeck, 2003). Based on this evidence we discard the first possibility.

Second, modulation of hIPS activity by increasing WM load was smaller for number conditions than for letters conditions. This may be interpreted as follows: Cell assemblies in the hIPS that code numerical magnitude/sequential order get activated by numbers automatically. WM processes do not induce additional activity in the remaining neural circuits in the hIPS when WM load increases. For letters these cell assemblies in the hIPS are not activated automatically, thus overall activity in the Letter Identity task Lag 1 (LIL1) condition is
smaller than in the NIL1 condition (see Table 13). However, when WM load increases WM related neural circuitry in the hIPS is involved to a comparable extent as for number specific conditions. However, the relative difference is larger for letter specific contrasts, resulting in hIPS activity in this interaction contrast \([(LIL2 – LIL1) – (NIL2 – NIL1)]\). Interaction contrasts reveal the difference in relative activation that was observed in the constituting simple contrasts (e.g. \((LIL2 – LIL1)\) and \((NIL2 – NIL1)\)). Thus, the ROI activity in the interaction contrast \([(LIL2 – LIL1) – (NIL2 – NIL1)]\) may mean that the relative difference is higher in contrast \((LIL2 – LIL1)\) as compared to \((NIL2 – NIL1)\). The Interaction contrast then provides indirect evidence for recruitment of different neural cell assemblies within the same ROI in two different kinds of processing.

The interaction contrast in the comparison task did not reveal hIPS activity in either of both possible directions. This might be due to the hIPS being activated to a similar degree for both letters and numbers. This means in turn that comparing the relative position of two letters in the alphabet activates brain areas overlapping with those activated when two numbers have to be compared in terms of numerical magnitude. This is in line with results observed by Fias and colleagues (2003) and supports the claim of common neural metrics for different kinds of magnitudes (Walsh, 2003). In similar vein, Marshuetz (2005) reported that the activity of the left parietal cortex was a function of interitem distances in the context of a paradigm examining order memory. The PC activity in contrast \([(NCL2 – NCL1) – (LCL2 – LCL1)]\) was located in posterior, superior parietal lobe (BA 7; PSPL) which is thought to be involved in storage processes in the context of WM tasks and attentional orienting (Dehaene et al., 2003) rather than representing numerical information. In more detail, studies have revealed functional activation in superior parietal cortex when participants shift attention in space (e.g. Vandenberghe et al., 2001; Wojciulik & Kanwisher, 1999). The peak activations reported above do indeed coincide very well with those reported by Vandenberghe and colleagues (2001) who asked the participants to keep attention engaged on an object that changed its position in space. Similarly, Lepsien and colleagues (2005) report activity in the superior parietal cortex when participants oriented spatial attention to the contents of working memory in a paradigm using retro cues, i.e., the cues appeared only after the stimuli disappeared. This result is remarkable since it demonstrates the importance of spatial attentional processes in the context of a working memory paradigm.

As recently pointed out, the mental representation of numerical magnitude is also related to the representation of space (Dehaene et al., 2003). Thus, when participants had to compare two numbers for magnitude they had to refer to the position of the objects on the relevant dimension (i.e. mental number line) which may be similar to orienting in space. This seems to be more difficult for numbers than for letters when another stimulus was presented in the meantime (as is the case for lag 2) which itself activates a (third) position along the
mental number line. This may be interpreted in terms of an automatic interference caused by the third number’s magnitude representation that has to be “overpowered” by additional attentional effort in order to decide which of two numbers is larger. Analyses of second order distance effects in the RT data in the 2-back condition seemed to be consistent with this interpretation. While an increasing distance between intermediate stimulus (n = 1; distractor) and the actual response-relevant stimulus facilitated responses, the opposite is true for the distance between distractor and the stimulus presented two trials before (n = 27; see Footnote 7 for details). Our results then seem to support the notion that the numerical magnitude representation bears resemblance with a spatial (and a temporal) dimension (Dehaene et al., 2003; Walsh, 2003). Similarly, Li and colleagues (2004) found the left DLPFC (TC: -46, 17, 27) to be more active when participants had to shift attention along a sequence of three categories for which participants had to update the number of respective items when presented with a series of items as compared to non-shift trials. Some of the PFC activity observed in the interaction contrast [(NCL2 – NCL1) – (LCL2 – LCL1)] is close to these coordinates (TC: -32, 21, 25). In line with this interpretation we observed activity in anterior cingulate gyrus (TC: -16, 6, 37; BA32/24) which recently has been linked with focusing attention on task-relevant stimuli which helps to resolve interference from distracting events (Weissmann et al., 2005). This also lends support to an attentional interpretation. Additional evidence comes from the behavioural data: We found an RT advantage for numbers as compared to letters when WM load was low and the task requires processing of magnitude/sequence information, i.e. conditions NCL0 and NCL1 were responded to faster and more accurately than corresponding letter conditions (LCL0 and LCL1, see Figure 1). However, when WM load increased, this advantage vanished. The fact that brain areas which

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7 One approach of investigating the interaction of WM and averbal semantics is to test the interaction of lag effect (WM load) and distance effect (semantics) in a 2 X 2 X 2 repeated measures ANOVA comprising the factors stimulus type (letter vs. number), lag (L1, L2) and distance (small: 1-3; large: 4-8) for each task separately. The results seem to imply a semantic influence of magnitude/sequence information in the context of a vWM task. Most importantly, for both tasks we observed an interaction between lag and distance (both F(1, 12) > 9.4 both p < .05). However, for a systematic and controlled investigation of such distance effects, one would need a much larger sequence of trials than the 14 trials used in each condition in this study. Especially we did not control for second order distance effects in lag 2 conditions, i.e. a modulation of RT due to the distance between the actual response-relevant stimulus (stimulus) and the intermediate stimulus (distractor), as well as the distance between distractor and the stimulus seen two trials prior (target) and the relation between these distances. Very similar second order congruency effects have been obtained in other attentional paradigms (Nuerk, Bauer et al., 2005) and may also be observed in working memory tasks. The results of this small and yet not systematically controlled stimulus set seem to indicate that RT is indeed differentially modulated by these distances and their congruity relation.
are involved in spatial attention are active in the context of a vWM task at least casts some doubt on the adequacy of numbers as stimulus material for the assessment of vWM.

In sum, the impact of numerical/sequential meaning depends on the task executed: In an identity match task little behavioural impact of the automatically activated number representation has been observed. For the comparison task our results imply a different role of numerical meaning in vWM: With low WM load numerical meaning assists performance when participants have to compare several items according to their magnitude and at the same time have to manipulate the sequence of items repeatedly. It interferes with the vWM task with increasing WM load. From a broader perspective this can be summarized by stating that numerical meaning, which is automatically activated whenever numbers are presented – regardless of the task at hand –, does indeed influence WM performance. A small but significant impact of semantic content of stimulus material on verbal WM processes is in line with the results of Neely and LeCompte (1999). Our results then are not in line with the postulate of a purely phonological code of vWM (e.g. Baddeley, 1966, 2003; Gisselgard et al., 2003).

6.3.2 Is the hIPS Stimulus-Driven and Number Specific?

Before we discuss the implications of our results with regard to the hypothesis of increased hIPS activity in the context of tasks that explicitly address magnitude/alphabetical order processing we refer to the claim of the hIPS being stimulus-driven and number specific (Eger et al., 2003): Only by computing interaction contrasts we were able to disentangle WM specific from stimulus material or task specific contributions to the activity in hIPS. Both vWM and number processing rely on the hIPS. This leads to the question of stimulus or domain specificity of the hIPS activity for number processing when using fMRI methods: Doubts about number specificity of the hIPS activation arise when taking into account the brain activity induced by letters as compared to numbers. Bilateral hIPS involvement was observed in comparison task specific contrasts where number conditions were subtracted from letter conditions. These activations might be attributed to accessing some kind of mental metric (Walsh, 2003) which is less automatic for letters than for numbers although SNARC effects (indicating automatic access to a spatially organized ordinal sequence) have been found for letters, too (Gevers et al., 2003). This is not in line with the notion of hIPS activity being stimulus-driven and number- or domain-specific (Eger et al., 2003). Indeed, Shuman and Kanwisher (2004) have published a series of fMRI experiments where they failed to support the notion that activity in the hIPS is specifically linked to the domain of processing symbolic (and non-symbolic) magnitude. When looking at neuronal responses in the hIPS reported by Eger and colleagues (2003; their Figure 2) it becomes obvious that this region was well activated when participants were matching visually presented letters to a predefined standard (a task equivalent to our 0-back task). Thus, hIPS activity was not number-specific and
stimulus-driven. Instead, hIPS activity appears to be modulated by accessing some kind of magnitude/order code rather than being purely number specific. A similar view is expressed by Walsh (2003) who proposes a theory of magnitude (ATOM). According to Walsh the representation of time, space and quantity is located in distinct but overlapping regions in IPS. This is in line with our results that show a modulation of hIPS activity by the interaction of task, stimulus material and WM load. Note that questioning the specificity of a given brain region’s activity for certain cognitive functions is not necessarily at odds with the approach we employ for interpreting the fMRI data: While activity in a given area may be taken as a signature for a given process, e.g. hIPS activity indicates magnitude processing, this does not imply a one-to-one mapping of brain activity to cognitive functions. Postulating that hIPS activity is stimulus-driven and number-specific, however, does imply a one-to-one mapping we do not consider useful given the complexity of cognitive functions and the poorly understood mechanisms of implementation in the brain. So, rather than being stimulus-driven and number-specific, the hIPS seems to participate in a variety of processes, some of which refer to magnitude processing, some do not. Supportive evidence is provided by single cell recordings in monkeys (Nieder & Miller, 2004): They found number tuned cells, i.e. cells that respond most to a specific number while their firing rate decreases with increasing numerical distance of the stimulus from the preferred number, in wide parts around the monkeys’ hIPS, rather than one circumscribed “number spot”. More interestingly, they observed a large amount of neurons within hIPS whose responses were unaffected by numerical magnitude, i.e. they were not number specific or stimulus driven. Therefore we propose that WM and magnitude processing rely on neural circuits both located within the hIPS. Behavioural interaction of WM load and stimulus material in a comparison task might then be interpreted in terms of overlapping and interacting neural circuits rather than completely distinct systems.

6.3.3 Increased Activity in the hIPS when Processing Magnitude/Alphabetical Order?

What do our results imply with regard to the hypothesis that the hIPS activation should be increased whenever the context explicitly addresses numerical magnitude/alphabetical order?

No coherent evidence supporting this claim was found: While left lateralized additional activity in the hIPS was found in the main effect contrast C – I this activity can be attributed to letter specific conditions by analyzing each stimulus material separately: For letters (LC – LI) additional bilateral hIPS activity was observed. This activity supports Dehaene’s claim. When taking into account other activated brain areas in this contrast it becomes evident that additional hIPS activity must be seen in the context of a widespread network of activations. This network most likely is due to WM effort that is more pronounced in the comparison conditions as compared to identity match conditions (see also Figure 26A and Figure 26B). We propose that participants activate the ordinal position of a letter within the alphabet. This
representation is not activated as automatically as it is for numbers. Therefore accessing the letters’ alphabetical position demands higher amount of hIPS involvement as compared to the identity match task (and in fact as compared to the number magnitude comparison task). Thus, this additional hIPS activation again comprises aspects of both functions the PC is involved in: processing of numerical magnitude/alphabetical order and storing processes in the context of a vWM task. Additional hIPS activity due to the comparison task in letter conditions alternatively may be interpreted in terms of task difficulty. Comparing two letters according to their alphabetical position is far less familiar than comparing them in terms of identity or performing a numerical magnitude comparison. Therefore, ROI activity might simply reflect task familiarity or difficulty. However, Barch and colleagues (1997) have shown that regions differentially responsive to task difficulty include inferior frontal Cortex and anterior cingulate Cortex but not PC. PC activity in their study was a function of WM demands. Similarly, Kondo and colleagues (2004) found a cingulo-frontal network differentially activated by task difficulty. PC activity on the other hand did not correlate with task difficulty but showed constant activity in all experimental conditions. Since task difficulty seems to modulate activity in brain circuits distinct from the ROI in the present study we do not consider it a good explanation for the present pattern of results.

In number specific contrasts the opposite pattern of results emerged. We observed additional activity in hIPS when subtracting comparison activity from identity match activity for numbers (NI – NC) while no hIPS activity was present in contrast C - I. This hIPS activity cannot be attributed to some automatic aspects of numbers being activated in the identity match task only, since this would hold for the comparison task, too. Instead, we suggest this to be indicating stronger WM activity. WM specific processes such as storage are known to rely on PC. Behavioural evidence suggests that for numbers in low WM load conditions a magnitude comparison is easier to perform than an identity match. This might be due to the fact that participants can refer to the semantics of numbers. This improves performance for low WM load conditions while interfering with WM performance at high WM load. In identity match task this semantic influence of numbers on performance is smaller resulting in a smaller benefit for the participants. Therefore additional WM capacities are employed when solving the identity match task at low WM load. WM and especially storage aspects of WM processes are well known to activate the hIPS (Chen & Desmond, 2005).

To sum up, while Dehaene’s hypothesis was - to some degree - confirmed for letters irrespective of WM load, for numbers it was not. Here the opposite seems to be true: hIPS gets activated to a higher degree when participants do not benefit from accessing a mental number line, i.e. under these conditions hIPS activity is not indicative of number specific processing. Instead it indicates additional involvement of WM related processes.
In conclusion we want to question the assumption of a purely phonological code of processing in verbal WM. Numbers activate a verbal semantics even in tasks not explicitly addressing the magnitude dimension. This semantic influence seems to be small but significant. Moreover it is modulated by WM load and the task performed. The semantic impact of numbers seems to be negligible and if any assists task performance in common n-back tasks that refer only to the identity of the stimuli. The influence of numerical semantic becomes more evident in tasks that explicitly address magnitude information. Here its influence clearly varies with WM load: For low WM load numerical magnitude assists task performance but it interferes at high WM load. Thus, it seems at least questionable whether numbers should serve as stimulus material for assessing purely verbal WM. Activity of brain areas involved in spatial attention adds to doubts concerning the adequacy of numbers as stimulus material for the assessment of vWM. We did not find converging evidence for Dehaene’s hypothesis of increased hIPS activity in (number processing) tasks explicitly addressing magnitude. Activity in hIPS was modulated by task, WM load and stimulus material. This questions the assumption of hIPS activity being number specific and stimulus driven (Eger et al., 2003).
7 Future Directions

This final section will briefly delineate which of the results of the current thesis may contribute to future studies.

First, the time-course of the magnitude comparison process for two-digit numbers remains unclear. That is, at which point of time does unit information influence the overall process? This should be further investigated by combining imaging techniques like fMRI with cognitive neuroscience techniques that offer a better temporal resolution like TMS and event-related potentials (ERPs).

Second, only very few attempts have been made to further investigate the extent to which the reported features of the mental representation of two-digit numbers are unique to (i) the Western cultures employing a left-to-right writing direction or (ii) the German language with its inversion of unit and decade naming for two-digit numbers (cf. Nuerk, Weger et al., 2005). For example, one may argue that the compatibility effect relies on the specific numerical systems and its partial incoherencies. Instead, the comparison of the compatibility effect in different notations and language contexts in a within-participant design examining bilingual persons speaking German and Chinese, for instance would allow to make more general claims about the mental representations of two-digit numbers. Note that the number naming system in China is extremely regular and reflects the place-value logic in a one-to-one mapping.

Third, in Study 4 it was claimed that the numerical meaning of numbers in ostensible non-numerical tasks compromises the assessment of purely verbal working memory. Further investigations are needed to systematically manipulate the numerical distances in an n-back task in order to make more profound statements about the interaction of verbal working memory functions and numerical semantics.

Fourth, numbers seem to influence working memory performance by their numerical meaning which is thought to be activated automatically. This may be the case only in situations that either require a magnitude judgement or allow for a conscious processing of the numbers by a temporally extensive presentation mode. Some evidence exists that bolster the claim of an automatic activation of numerical semantics in non-semantic, unconscious contexts (Dehaene et al., 1998; Naccache & Dehaene, 2001). By employing priming and masking techniques, this postulate may experience further corroboration.

Fifth, it was argued in favour of a relative hemispheric specialization with regard to the processing of decomposed versus holistic magnitude information. Clearly, further TMS and fMRI investigation are needed to clarify this issue more systematically. To my knowledge, no study has systematically varied left and right parietal and prefrontal TMS in a within-participant design so far. This design would allow disentangling the separate contributions of the proposed neural systems to the magnitude comparison process.


REFERENCES


Danksagung:

Es gibt eine ganze Reihe von Menschen, die mich im Laufe meiner Zeit in Aachen und bei der Erstellung dieser Dissertation in der einen oder anderen Weise unterstützt haben. Diesen möchte ich hiermit meinen tiefen Dank aussprechen.


In anderer Weise, aber nicht weniger wichtig hat Hans-Christoph Nürk mich stets unterstützt und zu Höchstleistungen angetrieben, sei es fachlich, bei der Erstellung diverser Anträge oder privat, bei der Auswahl des perfekten Bundesliga-Manager-Teams. Auch fand ich in ihm immer einen hilfreichen und wegziehenden Ratgeber in vielerlei Hinsicht, weit über das berufliche hinaus. Dafür mein aufrichtiger Dank!


Guilherme Wood danke ich – neben den fachlichen Gesprächen und den Rutschpartien auf Brixener Skipisten (natürlich ohne Skier) - für die unglaubliche (Belo) Horizont(e)erweiterung, was meine kläglichen Brasilienkenntnisse angeht.


Ich möchte mich bei den Kollegen aus dem IZKF (René Vohn, Ralph Schnitker) bedanken, die mich immer vortrefflich bei Fragen rund um die durchgeführten fMRI-Studien beraten haben. Mein spezieller Dank gilt hier Jochen Weber, der so vieles möglich gemacht hat und mich stets für mein lausiges Einrücken der immer zu komplexen Presentationprogramme gerügt hat. Alles Gute in Maastricht!


Ich danke der gesamten BaNG (Elise Klein, Andi Schweizer, Marjolein Korvorst, Kathrin Dressel, Frank Domahs) für die tolle Zusammenarbeit.

Ich bedanke mich bei der Medizinischen Psychologie und speziell bei Herrn Gauggel für die wohlmeinende Unterstützung.

Ich danke Herrn Spijkers für die Unterstützung meines Promotionsvorhabens.

Natürlich darf in dieser Reihe mein werter Mitbewohner Andreas nicht fehlen, dem ich für die sehr nette Zeit des Zusammenwohnens danke. Leider waren meine Bemühungen, dich nach Paris zu bewegen nicht erfolgreich.


Ich danke meiner Familie für die Unterstützung meines eingeschlagenen Weges aus der Ferne. Ganz besonders natürlich danke ich meiner Oma (Maria Göß) und meiner Mutter (Ingeborg Knops), die mir erst das Studium ermöglicht haben!

Zu guter Letzt möchte ich der wichtigsten Person in meinem Leben danken: Simone.
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