Research Report

Categorical and coordinate spatial relations in working memory: An fMRI study

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ABSTRACT

Spatial relations within and between objects can be represented either coordinately or categorically. Coordinate representations concern metric and precise relations, and are strongly associated with right parietal cortex activity, while categorical representations relate to more qualitative, abstract relations, and have shown to have a, somewhat weaker, relationship with left parietal cortex activation [Trojano et al., 2002. Coordinate and categorical judgements in spatial imagery. An fMRI study. Neuropsychologia, 40, 1666-1674]. In the current study, a functional magnetic resonance imaging (fMRI) experiment enabled a closer examination of this proposed hemispheric lateralization within a working memory paradigm. A visual half field task in a match-to-sample format was conducted to examine these lateralization effects with a short (500 ms) and a long (2000 ms) interval between two stimuli, with either a categorical or a coordinate instruction. In the behavioural data, the hypothesized hemispheric specialization was found for the brief interval. The imaging data support the hemispheric lateralization as well. The proposed lateralization effect is present during spatial relation processing, but only within the superior parietal cortex and with certain temporal constraints. Additionally, categorical trials show a clear involvement of the left and right premotor and posterior parietal areas during the brief interval, while coordinate trials are related to higher activity in the left and right insula, during the long interval. We propose a refined view on lateralization of spatial relation processing, keeping in mind the temporal restrictions shown by this study.

1. Introduction

In order to interact with our spatial environment it is critical to be aware of the locations of objects, not only in an absolute sense but also relative to other objects and ourselves. This enables us to navigate accurately through space and to communicate about our environment. Spatial relations be-tween objects can be classified into two types; categorical and coordinate spatial relations, as first proposed by Kosslyn (1987). Categorical relations can be expressed by prepositional, abstract labels such as above/below and right of/left of. Coordinate relations are more precise and metric and can be expressed in absolute measures of distance. Along with this classification, Kosslyn (1987) and Kosslyn et al. (1989)

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proposed a distinct difference in hemispheric processing. Categorical relations are thought to be processed predominantly by the left hemisphere, whereas the right hemisphere is assumed to be mostly concerned with coordinate relation processing. These hemispheric advantages are suggested to be due to the linguistic characteristics and involvement in navigation of the left and right hemisphere respectively, which are functionally linked to the preferred types of processing. Later simulation studies on this lateralization suggest a dominant role of receptive field sizes. Relatively large and overlapping field sizes are related to coordinate processing, while relatively small receptive field sizes are more suitable for categorical spatial processing (Chabris and Kosslyn, 1998; Jacobs and Kosslyn, 1994; Kosslyn et al., 1992).

Evidence for the foregoing functional lateralization has been found in many different experiments (see Jager and Postma, 2003), including a large number of visual half field experiments on healthy subjects (Christman, 2002; Hellige and Michimata, 1989; Laeng and Peters, 1995; Rybash and Hoyer, 1992) and patient studies (Laeng, 1994; Palermo et al., 2008). In the majority of these studies the proposed hemispheric dissociation was demonstrated. In particular, a right hemispheric advantage for coordinate tasks has been reported most often (for a review see Jager and Postma, 2003). These results have been found for studies focusing on perception (e.g. Hellige and Michimata, 1989; Rybash and Hoyer, 1992) and working memory (Laeng and Peters, 1995; Van der Ham et al., 2007) as well as on mental imagery (e.g. Palermo et al., 2008). Additionally, computer model simulations have indicated that the computation of coordinate and categorical relations is performed better by separate networks (Baker et al., 1999, Kosslyn et al., 1992). Apart from these confirming results, the left hemispheric advantage for categorical tasks is found less often and the idea of a complete double dissociation has been rejected by some (Niebauer, 2001; Sergent, 1991).

Remarkably, the number of direct neurophysiological and imaging studies addressing the distinction is limited. The only EEG study focusing on spatial relation processing offered a more critical view on this double dissociation (Van der Lubbe et al., 2006), proposing that differences between categorical and coordinate processing are mainly of a quantitative nature, caused by differential difficulty, than a qualitative one. Nevertheless the hypothesized lateralization effect has been found to some extent in a PET experiment for rather extensive networks of activation, including parietal and frontal regions (Kosslyn et al., 1998). An rTMS study has also provided proof for this lateralization pattern. Trojano et al. (2006) reported the hypothesized dissociation in the left and right parietal cortex involvement during categorical and coordinate processing. Stimulation of the left parietal cortex affected categorical processing and reduced the categorical learning effect during coordinate processing, whereas right parietal stimulation affected only the coordinate task.

So far, two fMRI studies (Baciu et al., 1999; Trojano et al., 2002) have shown that an increase in activity in the left and right parietal cortex was related to categorical and coordinate relation processing, respectively. While Baciu et al. (1999) report lateralization for the angular gyrus, Trojano et al. (2002) propose that the superior parietal lobule holds a central role in lateralized spatial relation processing. Additionally, Baciu et al. (1999) noted that the initial right hemispheric advantage found for coordinate processing decreased and eventually changed into a left hemispheric advantage in the angular gyrus, probably due to a practice effect, which caused categorization in the coordinate trials. Not only the parietal cortex seems to be of importance, there are some reports focusing on frontal areas, showing similar lateralization patterns (e.g. Slotnick and Moo, 2006) and others with a focus on larger parieto-frontal networks (Kosslyn et al., 1998).

In a more recent fMRI study Martin et al. (2008) made use of a working memory paradigm, in contrast to the older studies reported here, which have focused on perception in designs entailing single stimulus presentation (Baciu et al., 1999; Kosslyn et al., 1998) or on mental imagery (Trojano et al., 2002, 2006). This working memory paradigm enabled Martin et al. (2008) to examine memory load by changing the number of spatial relations to be remembered, which served as a measure of task difficulty. Accordingly, their imaging study lent support to a different view on spatial relation processing: the continuous spatial coding hypothesis. This proposal entails that both hemispheres are involved in categorical and coordinate relation processing, while factors as attentional and executive processes affect the balance between left and right hemisphere involvement. In particular, higher task complexity would lead to the recruitment of more right hemispheric resources. Coordinate spatial relation processing tasks, being typically more difficult, thus would show a right hemispheric lateralization. However some objections can be made to the idea of continuous spatial coding. The issue of task difficulty has been addressed previously and variation in task difficulty did not affect the direction of lateralization in these studies, only the extent of the difference (Kosslyn et al., 1992; Slotnick et al., 2001). The lateralization thus might only be apparent when the task at hand is sufficiently demanding. Furthermore, the computational analyses mentioned earlier further support the separate coding hypothesis by showing that the use of two separate processing mechanisms is more efficient than the use of a single one (Baker et al. 1999, Kosslyn et al., 1992).

Evidently, the diverse outcome of the limited number of imaging studies indicates the need for more clarity on the issue. Some criticize the lateralization hypothesis, and even if the expected pattern has been found, the location where it would be most apparent in the brain is also a matter of debate. From the literature discussed above, two views emerge; either the two types of spatial processing can be dissociated and show distinguishable patterns of activation, or the two types of processing are actually different expressions of the same underlying mechanisms, influenced by task properties such as difficulty and involvement of spatial attention. In the first case lateralization differences are caused directly by the different characteristics of categorical and coordinate processing, while in the latter case, lateralization differences are assumed to arise from quantitative differences during task execution.

Within the current study we focused on a working memory paradigm, reported previously (Van der Ham et al., 2007), because that type of match-to-sample design combined with neuroimaging allows us to further separate the two views and may provide new insights in the processing of spatial relations. We have selected the cross-and-dot stimuli for this task, as we did in our previous studies, where the relation of a

dot to a cross has to be assessed, memorized, and compared to a second stimulus. The match-to-sample design overcomes some of the shortcomings of a simple, perceptual paradigm (see Van der Lubbe et al., 2006). More importantly, with this design we could manipulate the working memory demands by varying the temporal characteristics of the task, which permits the comparison of brain activation patterns between categorical and coordinate processing at different working memory conditions. Given the differential results at a behavioural level (Postma et al., 2006; Van der Ham et al., 2007) this variable was expected to have a substantial influence on brain activity during task execution and to provide for well comparable trial characteristics.

The comparisons of spatial relation type as well as temporal characteristics can be placed in the context of the two views on spatial relation processing. If the original hypothesis on lateralization (Kosslyn, 1987) is fully correct we would expect a clear categorical-left parietal cortex and a coordinate-right parietal cortex advantage, regardless of retention interval. However, if the continuous coding hypothesis is more accurate as proposed by Martin et al. (2008), we would expect to discover lateralization patterns affected mainly by working memory requirements and task difficulty. Arguably, increasing the retention interval length may lead to increased working memory load (Haxby et al., 1995). Additionally, an increasing involvement of working memory could instigate a stronger right hemisphere advantage (e.g. Jonides et al., 1993), regardless of instruction type (categorical or coordinate).

2. Results

2.1. Behavioural results

The task entailed a match-to-sample comparison of two sequential stimuli, with either a categorical or a coordinate instruction, and a 500 or 2000 ms interval between the two stimuli. The behavioural results are depicted in Fig. 1A and B. For the response times (RTs) the analysis revealed a main effect of retention interval, $F(1,15) = 12.10$, $p < .005$, indicating faster responses for the 500 ms interval condition, compared to the 2000 ms interval condition. Furthermore, the interaction of retention interval and instruction was significant, $F(1,15) = 22.02$, $p < .001$, categorical and coordinate trials are only significantly different for the 500 ms interval where responses are faster for the coordinate trials, no significant difference is found for the 2000 ms interval. The overall interaction of retention interval, instruction, and visual field is a trend level effect, $F(1,15) = 3.93$, $p = .066$, indicating the differential effect of retention interval on the hypothesized instruction by visual field effect.

The analysis on the error rates (ERs) showed a significant main effect of instruction, $F(1,15) = 157.14$, $p < .001$, where more errors were made in coordinate trials, compared to categorical trials. A significant main effect of visual field was also found, $F(1,15) = 8.49$, $p < .05$; more errors were made in RVF/LH trials than in LVF/RH trials. Additionally, the interaction of instruction and visual field was significant, $F(1,15) = 5.74$, $p < .05$, indicating a clear LVF/RH advantage for coordinate trials, and no significant effect of visual field on categorical trials.
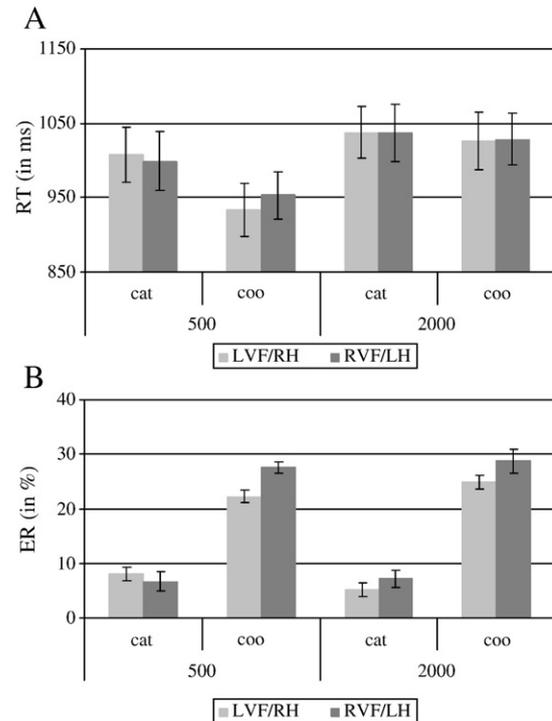

Fig. 1 – The mean values of (A) response time (RT) and (B) error rate (ER). Values are given for the left (L) and right (R) visual field (VF) and contralateral hemisphere (H) and error bars represent the standard error of the mean (SEM).

2.2. Imaging results

The voxel-based comparison for the factors categorical and coordinate combined, compared to rest led to the following bilateral ROIs, depicted in Fig. 2 and described in Table 1: Vermis, cerebellum, lateral premotor, superior and posterior parietal, middle occipital gyrus, insula, and medial premotor area ($p < .05$; corrected).

For all ROIs the mean regressor coefficients of categorical and coordinate separately were determined and subtracted. The resulting values are depicted in Fig. 3A through D, both categorical and coordinate data are reported separately as well as the difference between the two (categorical–coordinate), where a positive value indicates a higher contrast value for categorical than for coordinate, and a negative value specifies the opposite. Bonferroni-corrected one-sample t-tests were used to determine whether or not the difference values were significantly different from 0.

The categorical contrast was significantly larger than the coordinate contrast in the following areas for the 500 ms interval: lateral premotor right ($p < .05$), lateral premotor left ($p < .001$), superior parietal left ($p < .05$), posterior parietal right ($p < .01$), and posterior parietal left ($p < .001$). In the 2000 ms interval, the categorical contrast was significantly larger than the coordinate contrast in superior parietal left ($p < .05$) and posterior parietal left ($p < .001$), and significantly smaller than the coordinate contrast in superior parietal right ($p < .05$), insula left ($p < .01$), and insula right ($p < .01$).
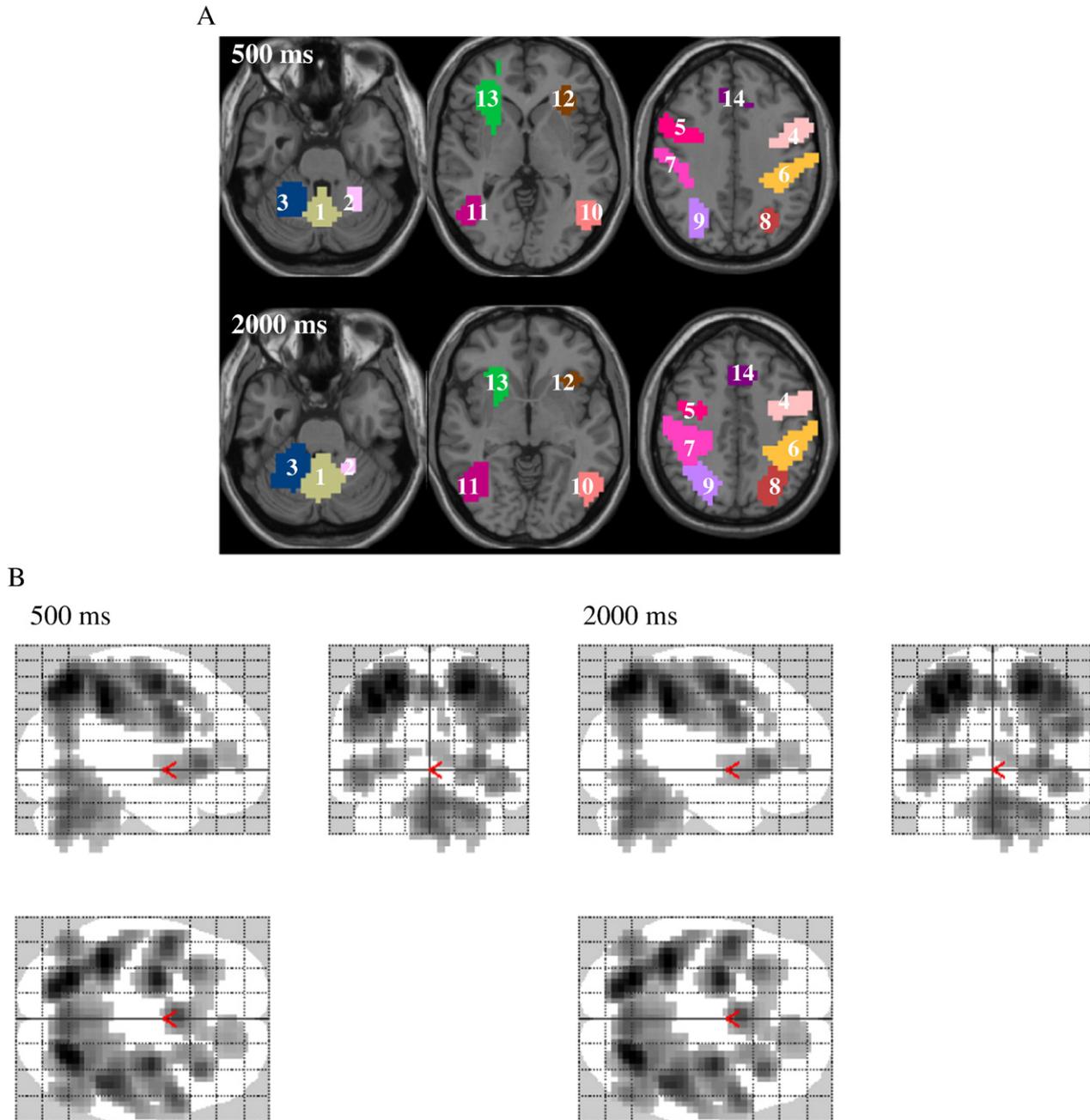
A

B

Fig. 2 – (A) The locations of all 14 regions of interest (ROIs) for both the 500 and 2000 ms trials and (B) cortical regions activated for the 500 and 2000 ms conditions.

3.   Discussion

Although behavioural evidence on a double dissociation between categorical and coordinate spatial relation processing is widespread, some have criticized these findings. Thus far, very few studies provided direct measures of brain activity to test the finding that categorical relation processing holds a left hemispheric advantage, while the right hemisphere shows an advantage for coordinate processing. An alternative for this double dissociation view is the proposal by Martin et al. (2008)

that lateralization is mainly caused by experimental factors like difficulty and required spatial attention, regardless of whether a categorical or coordinate task is presented. With the current study we addressed this issue with fMRI data on a cross-dot paradigm, presented with both a 500 ms and a 2000 ms retention interval.

The behavioural data indicated that overall the categorical trials yielded more accurate responses, while faster responses were given for coordinate trials, but only for the brief interval. The interaction of instruction*visual field was significant for ER and the retention interval*instruction*visual field inter-

Number	ROI	x,y,z	No. of voxels	Brodmann	Mean Z
Table 1 – All ROIs with MNI coordinates of peak values for the 500 and 2000 ms interval conditions separately.					
500 ms					
1	Vermis	4,−64,−20	273	–	7.15
2	Cerebellum right	28,−48,−28	171	–	6.93
3	Cerebellum left	−24,−48,−24	24	–	5.40
4	Lateral premotor right	32,−8,56	406	6	7.92
5	Lateral premotor left	−28,−4,56	460	6	7.93
6	Superior parietal right	44,−36,48	328	40	8.03
7	Superior parietal left	−40,−40,52	407	40	8.90
8	Posterior parietal right	24,−68,52	454	7	9.79
9	Posterior parietal left	−24,−64,60	325	7	9.77
10	Middle occipital gyrus right	52,−56,−8	167	20	7.04
11	Middle occipital gyrus left	−48,−64,−4	133	37	7.12
12	Insula right	32,24,4	273	45	6.40
13	Insula left	−28,28,4	87	45	6.29
14	Medial premotor area	0,8,52	103	6	6.31
2000 ms					
1	Vermis	4,−64,−20	436	–	7.64
2	Cerebellum right	28,−52,−28	268	–	6.73
3	Cerebellum left	−20,−48,−24	18	–	5.26
4	Lateral premotor right	32,−8,56	357	6	7.80
5	Lateral premotor left	−24,−4,56	407	6	8.15
6	Superior parietal right	44,−36,52	444	40	8.23
7	Superior parietal left	−36,−40,44	381	40	9.03
8	Posterior parietal right	24,−64,56	362	7	9.19
9	Posterior parietal left	−24,−64,56	301	7	9.86
10	Middle occipital gyrus right	52,−68,−4	144	19	6.49
11	Middle occipital gyrus left	−48,−64,−4	119	37	6.95
12	Insula right	32,24,4	148	45	6.68
13	Insula left	−32,24,4	113	45	6.32
14	Medial premotor area	0,8,52	187	6	6.40

The number of voxels, Brodmann area numbers, and mean Z scores are given for each ROI. The ROI numbers correspond to the numbers shown in Fig. 4.

action was at trend level for RT; which mainly confirms the right hemispheric advantage for coordinate trials, and only a slight left hemispheric advantage for categorical trials in the brief interval. These results support the lateralization hypothesis to some extent for the brief interval, but the lateralization is clearly stronger for the coordinate-right hemispheric advantage. These results are congruent with a previous report on this specific task (Van der Ham et al., 2007). It should be noted however, that for the brief interval, there seems to be a speed-accuracy trade-off effect for the difference between categorical and coordinate overall performance. This obscures the interpretation of the behavioural data to some extent, yet the lateralization pattern was not affected by it. Therefore, to eliminate such an effect in the imaging data, RT was introduced as parametric factor.

The imaging data indicated the involvement of a number of areas for both retention intervals. As expected, the superior as well as posterior parietal areas were of importance during both intervals. The regression coefficient was clearly larger for the categorical trials than the coordinate trials not only in the left superior and left posterior parietal cortex but also in the right posterior parietal cortex, in the brief interval. As the behavioural data have indicated, more errors were made in coordinate trials regardless of retention interval length. On the other hand, categorical trials showed a higher RT than coordinate trials in the short interval, yet

categorical performance itself did not change with retention interval length.

A clear indication of hemispheric lateralization was restricted to the superior parietal cortex for the long interval; the right area was significantly more active during coordinate processing, while the left area was significantly more active during categorical processing. The general involvement of the parietal cortex concurs with the previous studies described in the introduction (e.g. Baciu et al., 1999; Kosslyn et al., 1998). Also, the direction of the lateralization effect found here are in line with the predictions of the Kosslyn model. On the other hand, these findings do not simply confirm the idea that more difficult conditions yield more right hemispheric involvement, as discussed by e.g. Martin et al. (2008). Categorical performance does not differ between the two intervals, while the lateralization pattern does. In the imaging data, categorical trials seem to show overall lower contrast values for the right hemisphere areas for the long interval, compared to the brief interval. If anything, a reverse pattern would be expected for this comparison as the working memory demands could have increased for a longer interval (Haxby et al., 1995). However, for coordinate trials, there was an increase in the right superior parietal cortex when comparing the brief and long intervals, along with the assumed increase in difficulty with longer retention intervals. So for the coordinate trials we did find the right hemisphere
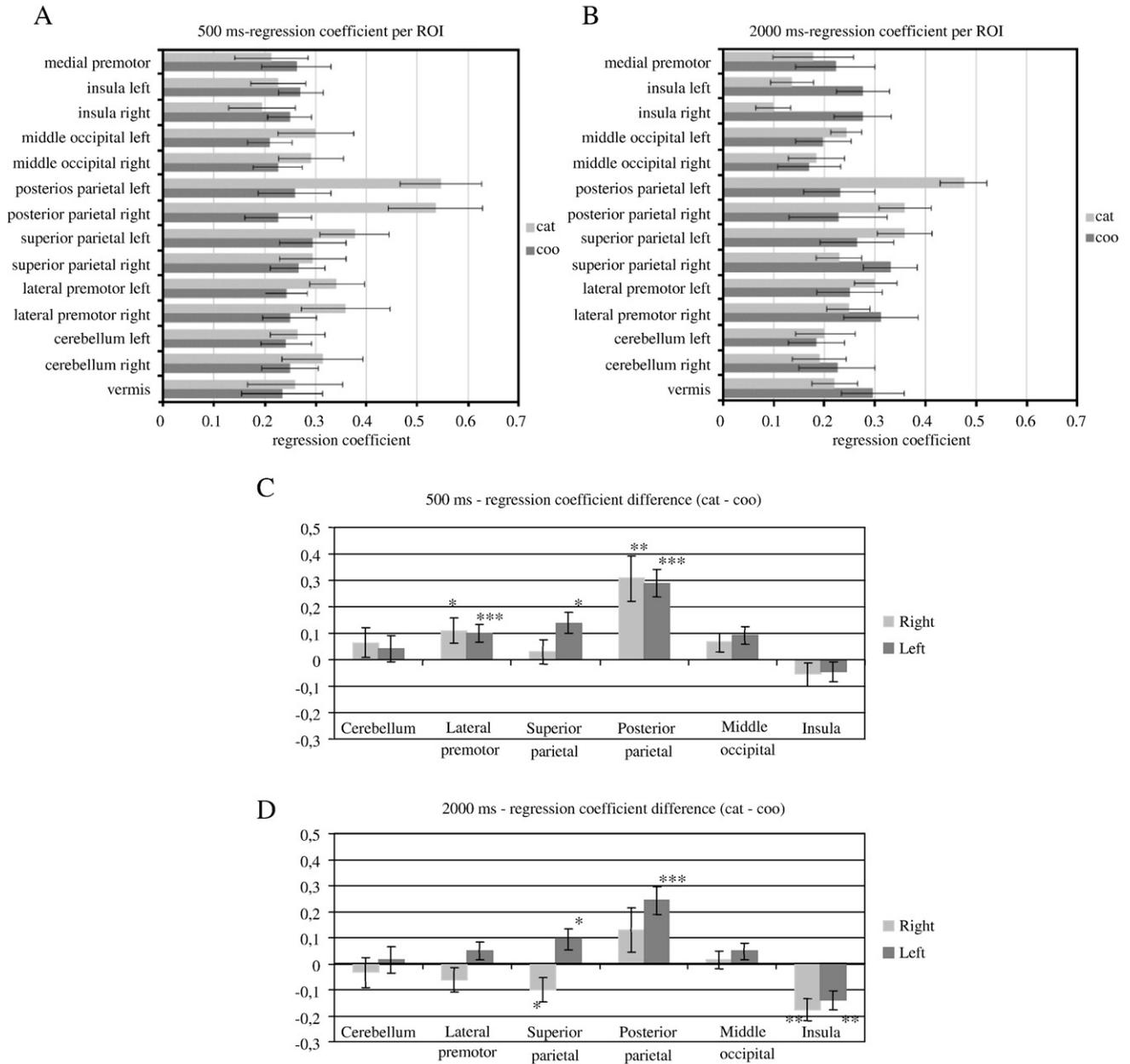
Fig. 3 – The mean regression coefficients of categorical and coordinate for all ROIs for (A) the 500 ms interval condition and (B) the 2000 ms interval condition. The mean difference in regression coefficient (categorical–coordinate) for the lateral ROIs in the left and right hemisphere for (C) the 500 ms interval condition and (D) the 2000 ms interval condition (a positive difference indicates a higher categorical coefficient, a negative difference indicates a higher coordinate coefficient). Error bars represent the standard error of the mean (SEM), left and right refer to hemisphere, *p<.05, **p<.01, ***p<.001.

increase along with a difficulty increase, while this was not the case for categorical trials. In short, the lateralization pattern is in accordance with the Kosslyn model, while the continuous coding hypothesis is only partially disproven.

The lateralization effect found for the superior parietal cortex agrees with the finding of Trojano et al. (2002) that a spatial transformation area is located within the superior parietal lobule. Furthermore, the right superior parietal cortex in particular appears to be involved in spatial forms of attention processing, and posterior parietal cortex activation of both hemispheres has been found to be related to a

combination of spatial perception, attention, and working memory (Coull and Frith, 1998).

In addition to the parietal areas, categorical trials also showed a greater contribution of the left and right lateral premotor areas compared to coordinate trials, for the short interval. The premotor area has been implicated in spatial processing. The left premotor area might also be implicated in inner speech during task execution (Smith et al., 1996), while right premotor area is thought to reflect spatial processing, both indicating the rehearsal of spatial information during the delay period in a working memory task (Smith

and Jonides, 1999). Given the trial composition in the present study, we would expect such activation during the delay period. Self reports have indicated a possible role of inner speech as a strategy to solve the cross dot task, mainly used for categorical trials (Van der Ham et al., 2007). Also, some have argued that the left hemisphere contribution to categorical processing is mainly a result of the verbal processes involved in the task (e.g. Kemmerer and Tranel, 2000), which might explain some of the left hemisphere activity found here. We wish to mention here that it appears nearly impossible to create a categorical task without any verbal characteristics, because it is inherent to categorical spatial relations that they can be adequately described by prepositions. Thus the verbal element in spatial categorization might be unavoidable.

The left and right lateral premotor cortex advantage for categorical trials restricted to the short interval is harder to explain. Perhaps the stimuli in the categorical trials require higher level processing to determine the category accurately. Due to the size of the cross, less immediate information on the category is available, while in the coordinate trials, the distance can be assessed directly and possibly more automatically. Category assessment might entail the elongation of the short arms of the cross, or some other adaptation, to determine the relative position of the dot, which might have led to the increase in RT. This additional processing could be reflected by the activation pattern in the premotor cortex.

The coordinate trials on the other hand were related to an increase in activity in the left and right insula, which was restricted to the long interval. The insula has been shown to be part of a network implicated in navigation (Ghaem et al., 1997). Since accurate coordinate information is essential to correct navigation (e.g. Bruyer et al., 1997; Jacobs and Kosslyn, 1994; Kosslyn, 1987) it is not surprising to see higher activation in the insula during coordinate processing, compared to categorical processing. The long interval might also be the situation in which more effort is needed to respond with metric accuracy, since this type of information decays over time (Huttenlocher et al., 1991; Werner and Diedrichsen, 2002) which might explain why this effect is only significant during the long interval.

Notably, the behavioural and imaging findings concerning lateralization are not fully congruent; the double dissociation is found for the short interval behaviourally, and for the long interval in the imaging data. A possible explanation for this difference is that the imaging data are an average of activity during six or nine trials, while the behavioural assessment focuses on lateralization effects present after the second stimulus presentation. As reported by Van der Lubbe et al. (2006) these trials can be divided in to three different stages: encoding, memorization, and retrieval; in the fMRI data, all three stages are represented. The behavioural data mainly reflect effects in the retrieval stage, because they are a direct response to the second stimulus, which is presented laterally.

Taken together, the present data appear to be more in favour of the original proposal of different processing systems for categorical and coordinate relation processing. Lateralization was found in the superior parietal cortex for the long interval condition; for categorical trials, more activity was found in the left hemisphere, while the right hemisphere was

more active during coordinate trials. Moreover, right lateralization of coordinate processing appears to correlate with difficulty, but such an effect is not found for categorical processing. The latter findings give mixed support for the alternative continuous coding hypothesis (Martin et al., 2008). Integrating the two hypotheses we may speculate that factors such as spatial working memory and perhaps spatial attention affect the degree, but not the direction of lateralization of spatial relation processing. Clearly they should be taken into account in future studies and when reviewing previous results.

4.   Experimental procedures

4.1.   Subjects

Sixteen subjects (eight females) participated in the experiment in exchange for course credit or a monetary reward. All subjects reported to be right-handed on the Edinburgh Handedness questionnaire (Oldfield, 1971), with a mean score of 87.7 (SD = 15.1) on a scale of –100 (extremely left-handed) to +100 (extremely right-handed). Informed consent was obtained from all subjects (approved by the Human Ethics Committee of the University Medical Centre Utrecht). All subjects were neurologically healthy, had normal or corrected to normal vision and were naive to the purpose of the experiment.

4.2.   Scanning protocol and apparatus

Scanning was performed on a Philips Achieva 3T scanner (Philips medical Systems, Best, The Netherlands) with a Quasar Dual gradient set. For functional scans, a navigated 3D-PRESTO pulse sequence was used (Ramsey et al., 1998; van Gelderen et al., 1995). The acquisition parameters were: TR = 22.5 ms (time between two subsequent RF pulses); effective TE = 33.2 ms; FOV(anterior–posterior, inferior–superior, right–left) = 224*256*160 mm; flip angle = 10°; matrix: 56*64*40 slices; voxel size 4 mm isotropic; 8-channel head coil; SENSE factors = 1.8 (left–right) and 2.0 (anterior–posterior). A new volume was acquired every 607.5 ms, and encompassed the entire brain. Immediately after functional scans, an additional PRESTO scan of the same volume of brain tissue was acquired with a high flip-angle (27°, FA27) for the image coregistration routine (see below). A T1 weighted structural image of the whole brain was acquired at the end of the functional runs.

The stimuli were presented by means of Presentation software (Neurobehavioral Systems, Inc.) on a PC. A rear projection screen and a video-projector system (frame rate 85 Hz) were used for stimulus projection. An MRI-compatible air pressure button box was used to record responses.

4.3.   Stimuli

The stimuli used in the current experiment were an adapted version of the cross-and-dot stimuli previously reported by Van der Ham et al. (2007). The stimuli consist of a black "+"-shaped cross (14*14 pixels/0.35°*0.35°) with a single black dot

(6 pixels/0.15° in diameter) on a white background. In Fig. 4 all possible dot positions are given; ten in each quadrant of the cross, placed at four equally different distances from the centre of the cross with the furthest placed at 45 pixels/1.13° from the centre. An important difference from the stimuli in our previous study is that the size of the cross has been reduced and the number of possible positions has been increased. A reduction in cross size decreases the difference in difficulty between the categorical and coordinate trials. The larger number of possible positions was implemented to reduce possible learning effects as has been reported for other stimuli, probably caused by familiarity with the range of possible locations (Rybash and Hoyer, 1992).

4.4.   Procedure

There were two different trial sequences; one with a 500 ms interval between the two stimuli and one with a 2000 ms interval. A single trial consisted of a central "×" shaped fixation cross (500 ms), followed by the central presentation of the first stimulus (S1) (150 ms), a blank screen (1500 ms, only for the 2000 ms interval condition), a second central fixation cross (500 ms), the lateral presentation of the second stimulus (S2) at 2.5° of visual angle from the centre of the screen (150 ms), ending with a blank screen during which subjects could respond (2000 ms). The first fixation cross was presented in red to indicate the start of a new trial. The second fixation cross was presented in grey to reduce interference with the following stimulus. The trial sequence with all durations for both interval lengths is given in Fig. 5A and B.

Prior to the scanning session all subjects practiced the task extensively. In total the experiment consisted of four blocks of trials, in which either the first and third were 500 ms interval trials, or the second and fourth. Subjects were informed about the interval length before each block started. The order of the blocks was pseudo-randomized over subjects; all possible different block orders were used. Within each block the three different instructions varied every nine trials in the 500 ms blocks and every six trials in the 2000 ms blocks. The first instruction was categorical, indicating that the quadrant of the cross in which the dot is presented, should be compared to

Fig. 5 – The trial sequence for trials with (A) a 500 ms interval and (B) a 2000 ms interval. S1 is the first stimulus, presented centrally, while S2, the second stimulus was presented laterally.
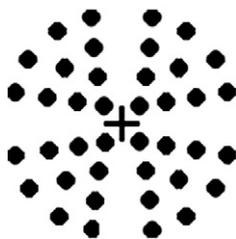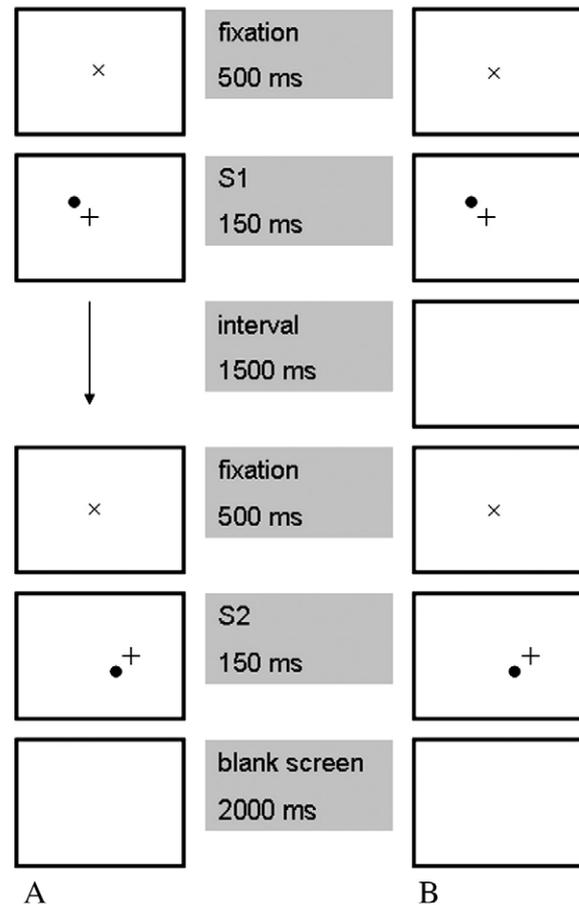

Fig. 4 – All possible dot positions in the stimuli used. There were four quadrants (i.e. categories) each containing 10 possible positions, and four different distances (i.e. coordinates) between the dot and the centre of the cross. A "match" response should be given when the dots in the two stimuli would appear within the same quadrant (categorical instruction) or with the same distance to the centre of the cross (coordinate instruction). Note that only one dot was displayed in a single stimulus.

the quadrant the dot is in for the second stimulus. This results in a "match" response when the dot is in the same quadrant as indicated by the arms of the cross and a "no match" response when the second dot is in one of the other three quadrants. The coordinate instruction also required a match/no match decision. Subjects were instructed to indicate whether the dot was at the same radial distance from the centre of the cross or not, disregarding quadrant information. They pressed the right button for a "match" response if the radial distance was identical and the left button for a "non match response" if the second dot appeared at one of the other three possible distances. The third instruction was rest, during which similar trials were presented, but subjects were asked to disregard all stimulus features and randomly select a button. The instruction was given by the presentation of a single word ("quadrant", "distance", and "rest") presented for 1000 ms prior to the six or nine consequent trials.

During each block, 1045 scans were made, for which the scanner triggered the start of the experiment. Each block with 500 ms intervals had a total duration of 630 s, and the blocks with 2000 ms intervals lasted 635 s. In the two blocks with a 500 ms interval a cycle of nine categorical trials (30 s), four rest trials (15 s), nine coordinate trials (30 s), and four rest trials (15 s) was repeated seven times. Thus, in total there

were 126 categorical, 126 coordinate, and 56 rest trials with a 500 ms interval. The cycle for the 2000 ms blocks consisted of six categorical trials (30 s), three rest trials (15 s), six coordinate trials (30 s), and three rest trials (15 s) and was also repeated seven times. This leads to a total of 84 categorical, 84 coordinate, and 42 rest trials with a 2000 ms interval. In SPM the categorical and coordinate blocks were specified and analyzed as 30 s segments, not at a single trial level. For all conditions, trials were balanced for visual field; 50% to the left visual field/right hemisphere, and 50% to the right visual field/left hemisphere. For both interval lengths, one block started with categorical trials and the other with coordinate trials.

4.5. Data analysis

4.5.1. Behavioural data
A repeated measure ANOVA was used to analyze all response times (RT) and error rates (ER). The conditions included in the analysis were retention interval (500 ms, 2000 ms) instruction (categorical, coordinate), and visual field (left, right), leading to a 2*2*2 design. Response times shorter than 200 ms and longer than 2000 ms were removed from the analysis.

4.5.2. Imaging data
All preprocessing steps were performed using SPM5 (http://fil.ion.ucl.ac.uk/spm/). After realignment, the functional scans were coregistered to the FA27 volume, using the first functional volume as a source. The structural scan was also coregistered to the FA27-scan, thereby providing spatial alignment between the structural scan and the functional volumes. Normalization parameters were estimated using the MNI T1-standard brain as template and the coregistered T1 volume as a source. All functional scans were then normalized and resliced to a 4×4×4 mm resolution. A 3D-Gaussian filter (8 mm full width at half max) was applied to all fMRI volumes.

A general linear model was used to estimate the task-related BOLD responses for each subject for both the 500 and 2000 ms tasks, with a high pass filter with a cut-off at 128 s, global scaling and AR(1) modelling of serial correlation in SPM5 with three regressors modelling onsets for instruction, categorical trial, and coordinate trial. The six realignment parameters were added as regressors to the GLM to remove residual motion related noise from the fMRI data.

The normalized response times of all trials (both categorical and coordinate) were used to generate a factor that could explain parametric modulations in the BOLD response as a result of intertrial differences in reaction times. This factor removes contrast activation between conditions as a result of differences in processing time. In addition, it removes unexplained variance as a result of intertrial response variation.

In the second level group analysis the following procedure was carried out for both retention intervals separately. Bonferroni paired-sample t-tests were applied to the contrast estimate of categorical + coordinate versus rest. Results were corrected for multiple comparisons ($p < .05$, Family Wise Error), and a 3D watershed algorithm and anatomical landmarks were used to discriminate the regions of interest (ROIs) that were involved in both tasks. The resulting 14 ROIs are reported in Table 1 and Fig. 2. For each ROI the average regressor coefficients were calculated for categorical and coordinate trials separately, and the difference in contrast values between categorical and coordinate trials was calculated at single subject level, using the MarsBaR software.

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