A hippocampal–parietal network for learning an ordered sequence

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The dynamics of the neural network that underlies learning transitive structures of an ordered sequence remains poorly understood. To address this, in the present study we used fMRI to track the time course of transitive inference learning. The hippocampus and the angular gyrus were each shown to be closely related to the learning trajectory, but differentially so. Hippocampal activity was shown to consistently increase with learning but no correlation was found between performance and hippocampal activation, suggesting a general role for the hippocampus. Left angular gyrus activity was also found to consistently increase with training, but, in addition, correlated significantly with behavioral performance. This suggests an involvement of the angular gyrus in learning the ordinal associations between stimuli.

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Understanding the neural basis of reasoning, that is, the capacity to draw inferences, presents an important challenge for cognitive neuroscience (Houdé and Tzourio-Mazoyer, 2003). In the present study, we focus on transitive inference (TI) as a canonical form of inferential reasoning.

In a typical TI task, participants have to learn the ordinal structure of a sequence of stimulus elements on the basis of premises that consist of adjacent elements in the sequence. In the initial phase, participants learn the internal order of individual stimulus pairs (e.g., the premises A—B, B—C, C—D, and D—E). After reaching a high performance criterion, in the next phase, knowledge of the ordinal structure of the sequence is evaluated by asking the participant to infer the transitive relation between non-adjacent stimulus elements. From the premises A—B, B—C, C—D, and D—E, the relation between stimuli not presented together, for example, B—D, can be inferred. Importantly, this capacity for TI is not unique to human adults (e.g., Acuna et al., 2002a,b) but has also been observed in preschool children (Bryant and Trabasso, 1971), primates (Gillan, 1981; Treichler and Van Tilburg, 1996), rats (Davis, 1992), and pigeons (von Fersen et al., 1991; Weaver et al., 1997). The fact that the capacity for TI is widespread across species is consistent with the idea that it results from very simple model architectures (e.g., von Fersen et al., 1991; Couvillon and Bitterman, 1992; Siemann and Delius, 1998); it also suggests that TI has a long evolutionary history, possibly because of its high degree of behavioral relevance (e.g., in determining social dominance; Paz-y-Mino et al., 2004). It follows that TI should rely at least partially on basic and evolutionarily old neural mechanisms. Animal lesion studies confirm that TI critically relies on the hippocampus (HC). Rats with a hippocampal lesion succeed in learning to discriminate between two adjacent odors, but are unable to understand the transitive relation between them (Dusek and Eichenbaum, 1997). Although the involvement of HC in TI has been confirmed in humans using PET (Nagode and Pardo, 2002) and fMRI (Heckers et al., 2004; Preston et al., 2004; Greene et al., 2006), the exact role of the HC in TI is still unclear. Few studies have focused on the time course of HC activation while participants learn the premise pairs. In one study, HC was found to be active in the middle of the learning phase, but not at the end of learning (Nagode and Pardo, 2002). However, this study did not include a control task, and could not exclude slow wave artifacts. A different pattern of hippocampal activation was observed by Greene and colleagues (2006). They found an increase in hippocampal activation with an increase in performance over training blocks showing that hippocampus was most active at the peak of performance. However, both Nagode and Pardo (2002) and Greene and colleagues (2006) only examined the time course of HC during learning of the premises (e.g., B—C), but neglected to examine the time course of HC activations directly related to transitive inference.

Performance in the test phase of the TI task is often characterized by a distance effect between the elements in the ordered sequence. More specifically, drawing transitive inferences is easier and faster for B—E than for B—D. Although a few TI studies failed to find such a distance effect (Ellebogen...
et al., 2007; Moses et al., 2006), the distance effect is frequently observed in humans (Tzelgov et al., 2000; Colombo and Frost, 2001; Acuna et al., 2002a,b) as well as in primates (D’Amato and Colombo, 1989; Treichler and Van Tilburg, 1996), and rats (Ferson et al., 1991, Van Elzakker et al., 2003; Wynne, 1995). The distance effect indicates that participants do not progressively walk through the premises to find the correct answer (which would evoke a reversed effect of distance), but form an integrated representation of the stimuli in which the order relations between them is well established. Previous hippocampal–cortical computational models have proposed that this integrated representation is stored in associative cortical areas (Frank et al., 2003; O’Reilly and Rudy, 2001). It is, however, unclear in exactly which cortical areas this would be. A number of studies suggest the parietal cortex as a key area for storing ordinal representations. Indeed, studies on the processing of the most prototypical orders, namely, numbers, reveal strong involvement of the parietal cortex, more specifically intraparietal sulcus (IPS; e.g., Fias et al., 2003; Eger et al., 2003; Pinel et al., 2004). Although numbers are a special case of ordinal stimuli because they also carry cardinal meaning, decisions on other ordered stimuli, like the alphabetical order of letters, also revealed IPS activation (Fias et al., 2007; Fullbright et al., 2003, Marshuetz et al., 2006).

Clearly, numbers and letters are highly practiced sequences. In a recent study, Acuna et al. (2002a,b) also found parietal activation in a TI task with arbitrary geometrical figures in which the underlying sequence was acquired during training. Their locus of activation was not in the IPS, but in both the superior parietal lobe and the supramarginal (SMG) and angular gyrus (ANG) of the inferior parietal lobe (see also Goel and Dolan, 2001). This result suggests that the parietal cortex in general might be particularly good in storing orders. However, the studies involved contrasting a simple height comparison control task with a more difficult TI task, and thus, activation in parietal areas could have been the result of task difficulty or attention (Majerus et al., 2006; Winstein et al., 1997). Hence, the storage of newly learned ordinal sequences in the association cortex, with the parietal cortex as a likely candidate, remains to be determined.

To summarize, the present study is designed to further investigate the time course of HC during the acquisition of the ordinal relations in TI. Therefore, participants were asked to perform a TI task while they were being scanned. We argued that if HC is involved in TI, its activation should increase with increasing knowledge of the transitive relations. A second aim of the present study is to investigate where in the cerebral cortex ordinal knowledge is eventually stored; we propose parietal areas IPS, ANG, and SMG as possible candidates.

Materials and methods

Participants

Twenty-six participants (all male, right-handed, mean age = 23.1 years, ranging from 19 to 30 years) were recruited from Ghent University. All participants gave informed consent in a manner approved by the ethical committee and the trial bureau of the Medical Department of Ghent University. None of the participants had a history of neurological or psychiatric illness or had any bodily ferromagnetic materials. Participants received a monetary compensation of 25 Euros.

fMRI task design

Prior to scanning, participants were explicitly informed that the purpose of the experiment was to study the neural correlate of learning transitive sequences. After receiving instructions of the details of the experimental procedure, participants were prepared for scanning and were positioned into the scanner. Before the acquisition of the fMRI time series was activated, a structural image (see Data Acquisition for details) was obtained.

In order to study the gradual acquisition of the transitive relations, we designed our experiment such that the TI learning phase was regularly interrupted by a TI test phase. Furthermore, we included a control phase to control for task difficulty when looking for the brain regions involved in storing the ordinal knowledge. An outline of the whole experiment is presented in Fig. 1A. A session was divided into six blocks, each block containing four repetitions of a fixation, learn, test, and control phase. The experimental session began with a familiarization phase (120 s) in which the six figures to be learned in the first five blocks (training set) were shown at a random position on the screen to allow participants to become accustomed with the different figures. Before the sixth block, a new set of figures (novel set) was shown in a second familiarization phase. This novel set of figures was introduced to disentangle simple temporal effects, for example, changes in arousal or habituation, from learning effects. Participants were instructed to fixate on a fixation cross that remained on the screen throughout the whole session.

Each block consisted of four sequences, each with a fixation phase, followed by a learning phase, test phase, and a control phase. During fixation phases a white fixation cross was presented in the center of a black screen for 15 s. Prior to each of the learning, test, and control phases, a summary of the instructions for that phase was presented for the duration of a trial (i.e., 2.8 s). Trial duration was the same in the learning, test and control phases (2.8 s). A learning phase consisted of 10 learning trials. Each learning trial began with a fixation cross in the center of the screen for 200 ms. This was followed by the simultaneous presentation of a figure to the left and to the right of the fixation cross for 200 ms. Participants then had to press the left or right button depending on whether they thought the left or right figure was the hindmost in the order respectively. The response time (RT) limit was 2.4 s. After a response, or after the RT limit, feedback was presented in the form of a colored circle in the center of the screen on top of the fixation point that remained visible. Because the trial duration was fixed at 2.8 s, the duration of the feedback was dependent on the RT and was set to a minimum of 200 ms. There were three different types of feedback: a green circle indicated a correct answer, a red circle indicated an incorrect answer, and a blue circle indicated that no answer was given before the RT limit. Importantly, stimuli in the learning phase were adjacent pairs only. Each possible combination was presented once in each order (e.g., AB and BA), resulting in 10 different trials per learning phase (i.e., the pairs AB, BC, CD, DE, EF, BA, CB, DC, ED, and EF). A learning phase thus lasted 28 s. A learning phase was followed by a test phase. A test phase was similar to a learning phase but for two exceptions. First, no feedback was provided during the test phase. As a result, the RT limit was extended to 2.6 s. Second, only non-adjacent stimulus pairs were presented in a test phase. Trials containing anchor items (the first and the last figure in the order) were excluded in the test phase. The remaining six different stimulus pairs (i.e., BD, CE, BE, DB, EC, and EB) were presented
twice in each test phase. A test phase thus consisted of 12 trials; each test phase lasted 33.6 s. After each test phase, a sensorimotor control phase was presented. This control phase consisted of a one-back task. As in the learning and test phase, two figures were presented for 200 ms. The task was to remember both figures until the next trial, and to press the button corresponding to the side on which a figure of the previous trial appeared. The sensorimotor demands for this task match those of the test phase. Furthermore, a one-back task is expected to involve working memory. Using a one-back task as a control thus removes any activation related to sensory–motor, as well as working memory processes. The stimuli used in the control task were from a different figure set (control set). A control phase also consisted of 12 trials and thus lasted 33.6 s. After five blocks with the training set, the novel set of figures was introduced during the second familiarization phase. Then participants had to learn the sequence of these new figures through four repetitions (6th block) of the sequence of fixation, learning, test and control phase. Participants were informed of this change of figure set before entering the scanner, but were not told when it would take place. The set of figures used in the one-back task remained the same throughout the entire experiment.

**Stimulus presentation and response collection**

Participants were positioned head first and supine in the magnet and a mirror was placed for viewing a large projection screen at the back of the magnet bore.

Three different sets of stimuli, training set, novel set and control set, were created (see Fig. 1B). The stimulus sets were randomized between participants, as well as the order of the figures in a stimulus set. Stimuli were projected in white against a black background. Stimulus delivery and the recording of behavioral data were controlled by E-Prime (www.pstnet.com/eprime; Psychology Software Tools) running on a Pentium 4 laptop positioned outside the magnet room. The magnet room was darkened to allow easy visualization of the experimental stimuli. Participants responded by pressing magnet-compatible two-key response boxes with their left and right hands.

**Data acquisition**

Imaging was performed on a 3-T MRI system (Siemens 3T Trio) using a standard eight-channel head coil. Participants were instructed not to move their heads in order to avoid motion artifacts. To further restrict head movements, the participants’ heads were fixed into position by foam cushions. After automatic shimming of the magnetic field on each participant, a 3-D high-resolution T1 anatomical image was acquired for coregistration with the functional images (3-D MPRAGE, 176 slices, slice thickness=0.90 mm, in-plane resolution=0.9×0.9 mm², TR=1550 ms, TE=2.89). Next, for fMRI, a single-shot multiple slice T2*-weighted echo planar imaging (EPI) sequence was used with the following parameters: TR=2500 ms, TE=33 ms, flip angle 90°, in-plane resolution=3×3 mm, FOV=192 mm², matrix
dimensions 64×64, slice thickness=3 mm, interslice gap=1.5 mm. Forty sagittal slices covered the whole brain. The experiment consisted of one scanning session containing 1248 volumes.

Data analysis

Data processing and analysis were performed using Matlab and SPM2 (Wellcome Department of Imaging Neuroscience, Institute of Neurology, UCL; http://www.fil.ion.ucl.ac.uk/).

At a single-subject level, slice time correction was performed before motion correction. All images were coregistered with the participants' corresponding anatomical (T1-weighted) images, and realigned to the first volume. The resulting images were normalized using 12-parameter affine transformation into SPM2’s MNI EPI 3×3×3 mm template using the corresponding anatomical image as a reference, smoothed, using a 7-mm full width at half maximum Gaussian kernel, and temporally filtered (cutoff 128 s). Learning the order of the first stimulus set thus lasted 5 blocks, where the new figures were only learned for 1 block (see Fig. 1A). For each participant, condition-specific regressors were defined that modeled the time course of the experimental events: 18 regressors modeled the learning, test, and control phases in the six blocks; one more regressor modeled the images acquired during familiarization and presentation of the instructions. The BOLD response in each condition was modeled by convolving these neural functions with a canonical hemodynamic response function to form covariates in a general linear model.

Group analyses were performed according to the random effects procedure using the single-subject contrast images as input. Group SPMs were generated using a one-sample *t* test with a voxel threshold of *P*<.001. We calculated that in order to get a corrected *P* value of <.05, a cluster should contain 46 or more contiguous voxels. Thus, the activation maps were thresholded with a *t* value of 3.73 (*P*<.001), and a cluster size of >46 voxels (corrected *P*<.048). Regions of interests (ROI) were defined as the clusters resulting from the contrasts. Percent signal change (psc) for ROIs were analyzed using Marsbar 0.38 (Brett et al., 2002). Images were created using Caret (Van Essen et al., 2001).

Four participants were removed from the analyses because of motion artifacts. Six more participants were removed because they failed to learn the ordinal sequence (i.e., performance only reached 60% in the test or learning phases of the fifth block), or failed to perform the control task (i.e., average performance was only 60%). Although these six participants could potentially be interesting, the reasons why they failed to learn the sequence (lack of interest, fatigue, difficulty) are unknown. Therefore, their data were not analyzed. Reported *t* tests are two-tailed, unless stated otherwise; the significance level was set at α=.05.

Results

Behavioral results

Behavioral performance is shown in Fig. 2. A repeated measures ANOVA (Block: 1 to 6) on the mean accuracy showed a significant effect of block, *F*(5,80)=39.51, *P*<.001, MSE=164. Linear trend analyses showed a significant linear increase from block 1 to block 5, *F*(1,16)=205.86, *P*<.001, MSE=111. Furthermore, a significant decrease was observed from block 5 to block 6, *F*(1,16)=84.12, *P*<.001, MSE=165.

Imaging results

Because feedback-based learning of simple associations is not central to the questions addressed in the present paper, the fMRI data from the learning phases in the experiment were not analyzed further.

To investigate the areas involved in learning the transitive structure of the sequence of stimuli (ABCDEF), we studied the
time course of brain activation related to performance in the test phase of the TI task. We therefore contrasted the block with the highest behavioral performance (where the order is most strongly internalized; block 5) with the blocks with the lowest behavioral performance (where the order is least strongly internalized; blocks 1 and 6). This contrast was masked exclusively \((P < .01)\) with the same contrast (block 5 vs. blocks 1 and 6) performed on the control blocks to remove voxels that have the same activation profile but that are not specifically related to TI. Areas with significant activation included areas in the bilateral temporal lobes, bilateral paracentral lobes, left middle occipital lobe, and left and right HC (see Table 1 and Fig. 3A).

Percent signal change (psc) analyses of our regions of interest, that is, left and right HC, revealed a clear relationship with learning the TI task. A 2 (hemisphere: left or right) \(\times\) 6 (block: 1 to 6) repeated measures ANOVA on the psc data revealed a significant effect of hemisphere, \(F(1,15) = 5.67, P < .05,\) \(MSE = 0.042\): Activation was higher in the right HC, compared to the left HC. There was also a significant effect of block, \(F(5,75) = 4.00, P < .005,\) \(MSE = .050\). Linear trend analysis showed a significant linear increase from block 1 to block 5, \(F(1,15) = 22.30, P < .001,\) \(MSE = .040\). A significant decrease was observed between block 5 and block 6, \(F(1,15) = 6.28, P < .05,\) \(MSE = .059\). The absence of a significant interaction between hemisphere and block \((P > .2)\) indicates that the pattern of activation is similar for both hemispheres. Activation patterns of left and right HC in the test condition are shown in Fig. 3B.

To investigate how HC activation relates to behavioral performance, a correlation analysis was performed. A linear regression on the activation in left HC from block 1 to block 5 resulted in an intercept as a measure for overall activation (because regressors were mean-centered), and a slope as a measure of change in activation, per participant; the same analysis in right HC resulted in an additional intercept and slope value per participant. These values were correlated to the mean-centered intercept and slope from a linear regression on the behavioral performance from block 1 to block 5. As shown in Table 1, this analysis did not show any significant relation between HC activation and behavioral performance.

The reversed contrast, that is, contrasting blocks 1 and 6 to block 5, did not reveal any significant activation at a \(P < .001\) threshold.

As can be seen in Table 1, no parietal activation was observed at this threshold. However, removing the constraints of the cluster size revealed a small group of significant voxels \((n = 8)\) in the angular gyrus of the left parietal cortex.

A different way to determine brain areas involved in representing the ordered sequence ABCDEF is to contrast the test condition to the control condition in those blocks in which the test and control task are matched in terms of performance to control for a confound with difficulty. Because the test phase was significantly more difficult than the control phase in blocks 1 and 2 \((t\) test, both \(P < .01)\), they were eliminated from this analysis. Blocks 3, 4, and 5 were retained because, in these blocks, the test phase and the control phase were equally difficult.

By contrasting the test condition with the control condition in these three blocks, significant activations were observed in the parietal cortex (more specifically, the left angular gyrus [ANG]), frontal regions of the left hemisphere and bilateral precuneus (Table 2 and Fig. 4A). As can be seen in Fig. 4B, the time course of ANG activation closely resembles the pattern of behavioral performance and hippocampal activation.

To investigate the relation of ANG to behavioral performance, we calculated a slope and intercept for ANG activation. This revealed a significant correlation between the slope in ANG activation and the intercept of behavioral performance, \(r = .47, P = .038\) (one-tailed), indicating that more quickly increasing ANG activation throughout the experiment was related to better overall performance of the subject (see Table 3 and Fig. 4C).

The reversed contrast, contrasting blocks 3, 4, and 5 from the control phase to the test phase, revealed activation in the left precentral cortex \((-39, -3, 39)\), right frontal cortex \((33, -3, 51)\),

### Table 1

<table>
<thead>
<tr>
<th>Stereotaxic coordinates</th>
<th>No. of voxels</th>
<th>(t) value</th>
<th>Anatomical region</th>
</tr>
</thead>
<tbody>
<tr>
<td>((-54, -48, 12))</td>
<td>148</td>
<td>6.17</td>
<td>L Middle temporal</td>
</tr>
<tr>
<td>((-42, -63, 21))</td>
<td>48</td>
<td>4.78</td>
<td>L Superior temporal</td>
</tr>
<tr>
<td>((-54, -48, 9))</td>
<td>126</td>
<td>5.71</td>
<td>R Middle temporal</td>
</tr>
<tr>
<td>((-51, -42, 9))</td>
<td>126</td>
<td>5.30</td>
<td>R Superior temporal</td>
</tr>
<tr>
<td>((-6, -30, 63))</td>
<td>179</td>
<td>5.58</td>
<td>R Paracentral lobe</td>
</tr>
<tr>
<td>((-12, -30, 66))</td>
<td>126</td>
<td>5.13</td>
<td>L Paracentral lobe</td>
</tr>
<tr>
<td>((-39, -24, 15))</td>
<td>82</td>
<td>5.58</td>
<td>R Hippocampus</td>
</tr>
<tr>
<td>((-24, -18, 12))</td>
<td>74</td>
<td>5.13</td>
<td>L Hippocampus</td>
</tr>
<tr>
<td>((-27, -93, 12))</td>
<td>52</td>
<td>4.43</td>
<td>L Middle occipital</td>
</tr>
</tbody>
</table>

Coordinates are in MNI space. Clusters are labeled according to AAL (Anatomical Automatic Labeling; Tzourio-Mazoyer et al., 2002). L = left, R = right.
right occipital cortex (36, −72, 27), and both left superior parietal cortex (−27, −51, 51) and right superior parietal cortex (27, −54, 51).

Discussion

The results of this study showed that participants succeed in constructing a unified representation of the ordinal relation of the stimuli, as indicated by a behavioral comparison distance effect in the last test phases (blocks 4 and 5). As predicted, the acquisition of the ordinal relations was related to activation in the left and right HC, and the parietal cortex, in particular, the left ANG. By looking at neural responses across time, and by relating neural responses to behavioral performance, we obtained a more precise insight into the specific contributions of these two regions.

Our results confirm earlier observations that learning the transitive structure of a sequence of elements involves HC (Greene et al., 2006) and that the time course of hippocampal activation resembles the time course of behavioral performance. However, whereas Greene and colleagues (2006) found hippocampal activation in the learning phase to be a good predictor of behavioral performance in the TI test phase, we did not find a significant correlation across participants between hippocampal activation and behavioral performance. This divergence in results may come from differences between the current design and the design of Greene and colleagues (2006). First, we studied the role of the hippocampus in the acquisition of the transitive relations, and not during the acquisition of learning simple associations as in Greene and colleagues (2006). Second, participants were not...
informed about the ordinal relation between the stimuli in Greene and colleagues (2006), whereas our participants were explicitly instructed to learn the ordinal structure of a sequence of visual stimuli.

The fact that we do not find a correlation might indicate that the role of the HC in TI learning is not directly related to the successful construction of an ordered cognitive representation, but is more generally involved in encoding the stimuli. A plausible interpretation, in line with Marshaluetz (2005), is that the role HC has in TI is identical to the role it has for many other cognitive tasks, namely, pattern separation (e.g., Rolls and Treves, 1998; O’Reilly and Norman, 2002; Leutgeb et al., 2007). Pattern separation is the neural processing mechanism that makes the neural representation of similar stimuli more distinguishable by decorrelating input patterns and creating sparse, non-overlapping, neural representations. Applied to the current context, each stimulus to be learned activates a pattern of elementary features in the cerebral (e.g., extrastriate) cortex. Given the visual similarity of the different stimuli (see Fig. 1B), the activation patterns of different stimuli will be highly overlapping. This will make it very difficult to create the integrated representation of the underlying sequence because the high overlap leads to interference between the different stimuli. A solution to this problem can be obtained by pattern separation: If activation patterns are separated from one another, the interference problem will diminish or disappear, making the learning task much easier. Assuming that HC is an area that is specialized to perform pattern separation (e.g., Rolls and Treves, 1998; O’Reilly and Norman, 2002; Leutgeb et al., 2007), one would intuitively expect a decrease of hippocampal activation across time in our experiment, since sparse coding implies that less neurons are required to represent a stimulus than in the original neural representation of that stimulus. However, an increase is predicted if, as we assume, a sparse representation is gradually built up in HC while the non-sparse pattern is represented elsewhere in the brain. Consistent with our general interpretation of the involvement of HC in our study, a learning-related increase of hippocampal activation has been observed in TI tasks (e.g., Greene et al., 2006) and also in experimental paradigms (e.g., artificial grammar learning) that do not involve TI learning, but instead involve stimuli that are hard to separate (Strange et al., 1999).

We predicted that the construction of a stable cognitive representation would involve the parietal cortex. The profile of brain activation in the ANG of the left hemisphere confirms our prediction. In line with Acuna and colleagues (2002a,b), we found that ANG was more active in the test condition than in the control condition, even when the conditions were matched in difficulty. Although the locus of parietal activation in this study is different from intraparietal sulcus (IPS) activation typically found in number processing, it almost perfectly coincides with the left hemispheric ANG area that has been identified to play a crucial role in performing mental arithmetic. More specifically, ANG has been shown to be involved in the retrieval of arithmetic facts from memory (see Dehaene et al., 2003 for a meta-analysis). We believe that this overlap is not coincidental. In mental arithmetic, ANG activation is determined by the degree of involvement of language-mediated processes (Dehaene et al., 2003). Involvement of language-related processes is also supported by the lateralization to the left hemisphere. In line with this and with a recent suggestion for the role of the ANG in linguistic sequences (Hubbard et al., 2005), our participants reported having verbalized the stimuli in a post-scanning debriefing. Other tasks focusing on semantic associations of words also typically activate ANG (Demonet et al., 1992, 1994; Mummery et al., 1998; Price et al., 1997). Therefore, it is likely that linguistic labels for the different stimuli are created during the TI task and that the ANG is critically involved in this. Indeed, a significant correlation between the increase of ANG activation (slope) and overall behavioral performance (intercept) means that overall performance in the test phase is better for participants with faster ANG recruitment during the experiment. In other words, participants who quickly adopt a verbalizing strategy to learn the ordered sequence have an overall better performance in the task. However, this does not imply that TI is only acquired through verbal mechanisms, but highlights the importance of language as a learning aid.

Given that earlier studies (e.g., Fias et al., 2003, 2007) found IPS activation for ordered sequences, why did we not find any, but instead found more IPS activation in the control task than in the TI task? First, we note that this finding is consistent with earlier studies using newly learned sequences that also did not show IPS activation (Acuna et al., 2002a,b; Greene et al., 2006). Second, although there are, of course, other potential reasons for the comparison distance effect, it is known that a comparison distance effect can emerge in the TI task simply from associations between the stimuli and the appropriate response labels of the task (Frank et al., 2003; O’Reilly and Rudy, 2001; Siemann and Delius, 1998; Verguts et al., 2005). We therefore suggest that for newly learned sequences, the TI task is solved exclusively by using these associations. When stimuli are familiar (e.g., numbers, letters), a different kind (possibly, spatial) of representation is built (see also Moses et al., 2006), and the IPS is then possibly recruited. A direct prediction from this is that if a new stimulus sequence is trained much more extensively, IPS activation should gradually emerge; this remains to be tested.

In sum, the results of this study showed a hippocampal–parietal network involved in learning the correct order of arbitrary figures. By looking at the time course of the activation, we show that parietal (ANG) activation was not due to task difficulty, but rather, ANG activations suggest a crucial role for forming semantic associations between artificial stimuli. The pattern of activation in HC also revealed a relation to TI. We proposed that this might be due to the role of the HC as a pattern separator.

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