

# Neural Correlates of Artificial Grammar Learning

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**Artificial grammar learning (AGL) is a form of non-declarative memory that involves the nonconscious acquisition of abstract rules. While data from amnesic patients indicate that AGL does not depend on the medial temporal lobe, the neural basis of this type of memory is unknown and was therefore examined using event-related fMRI. Prior to scanning, participants studied letter strings constructed according to an artificial grammar. Participants then made grammaticality judgments about novel grammatical and nongrammatical strings while fMRI data were collected. The participants successfully acquired knowledge of the grammar, as evidenced by correct identification of the grammatical letter strings (57.4% correct; SE 1.9). During grammaticality judgments, widespread increases in activity were observed throughout the occipital, posterior temporal, parietal, and prefrontal cortical areas, reflecting the cognitive demands of the task. More specific analyses contrasting grammatical and nongrammatical strings identified greater activity in left superior occipital cortex and the right fusiform gyrus for grammatical stimuli. Increased activity was also observed in the left superior occipital and left angular gyrus for correct responses compared to incorrect. Comparing activity during grammaticality judgments versus a matched recognition control task again identified greater activation in the left angular gyrus. The network of areas exhibiting increased activity for grammatical stimuli appears to have more in common with studies examining word-form processing or mental calculation than the fluency effects previously reported for nondeclarative memory tasks such as priming and visual categorization. These results suggest that a novel nondeclarative memory mechanism supporting AGL exists in the left superior occipital and inferior parietal cortex.** © 2002 Elsevier Science (USA)

## INTRODUCTION

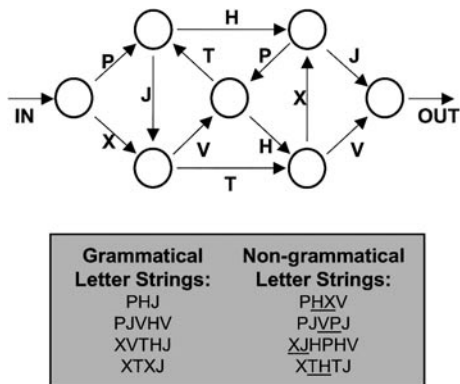
Declarative, or explicit, memory is conscious memory for facts and events and is supported by the medial temporal lobe (MTL; Squire, 1992, 1994). By contrast,

nondeclarative, or implicit, memory is a nonconscious form of memory which is intact in amnesic patients and functions independently of brain structures such as the hippocampus and the MTL (Squire *et al.*, 1993).

While many forms of nondeclarative memory involve the processing of simple sensory information (e.g., priming; Graf *et al.*, 1984) or the learning of motor skills (e.g., perceptual–motor sequence learning; Nissen and Bullemer, 1987; Reber and Squire, 1994), some forms such as artificial grammar learning (AGL) involve the nonconscious consolidation of complex rules and structures. AGL, which was first described by A. Reber (1967), typically involves exposing participants to letter strings generated from an artificial grammar structure without their being told the grammatical nature or underlying rules of the strings (Fig. 1). Subsequently, the existence of the grammar is divulged and participants are asked to judge whether or not a series of novel strings follows the same rules as those of the previously seen strings. Using this paradigm, healthy participants discriminate between grammatical and nongrammatical letter strings at a level better than chance. It is generally reported that participants rely on “intuition” or guessing when deciding whether the stimuli follow the same rules as those in the study phase, and participants are unable to consciously describe the specific structure of the grammar, even when they perform better than chance (Seger, 1994).

The type of memory that supports AGL has been shown to occur independently of the MTL (including the hippocampus). In several studies, (Knowlton *et al.*, 1992; Knowlton and Squire, 1994, 1996), it was shown that amnesic patients with damage to MTL structures exhibited normal performance on the AGL task. This was in contrast to a recognition control condition in which amnesic patients were impaired at distinguishing between old and new letter strings (i.e., patients could correctly assert whether or not a letter string was grammatical, but could not determine whether or not a string was previously seen). Additionally, several experiments have shown that individuals with damage to the basal ganglia, such as patients with Huntington’s and Parkinson’s diseases, also demonstrate normal AGL (Knowlton *et al.*, 1996; Reber and Squire, 1999).

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**FIG. 1.** Structure of the artificial grammar. Letter strings are generated by starting at the “IN” position and adding a letter at each transition according to the direction of the arrows until the “OUT” transition is reached. Examples of grammatical and nongrammatical strings (with the error transition underlined) are shown.

While neuropsychological data provide strong evidence that AGL is not subserved by either hippocampal or striatal learning systems, the exact neural substrate of this phenomenon is not known.

Several studies have attempted to ascertain the neural substrate of AGL via functional imaging. A traditional study test AGL paradigm was performed by Seger *et al.* (2000) in which participants studied grammatical letter strings and then made either grammatical or recognition judgments while fMRI data were collected. Compared to a baseline task, recognition activated the right prefrontal, precuneus, and medial occipital cortices, while grammar judgments lead to increases in the left prefrontal and bilateral occipital/parietal cortices. This network of activity bears some resemblance to results from an earlier pair of studies by Fletcher *et al.* (1999) and Dolan and Fletcher (1999). A novel AGL-like paradigm was utilized which deleted the study phase and instead had participants classify letter strings via feedback (after each grammaticality choice, participants were told whether or not they were correct). Since letter strings were repeated within blocks but were novel between blocks, it was argued that within-block judgments would represent recognition processes, while judgments made between blocks (at the beginning of the blocks) would rely on knowledge of the abstract rules. Recognition-based choices elicited a pattern of activity that included the right prefrontal cortex, while rule-based judgments lead to increases in the left prefrontal regions. However, given that participants were not told to make separate recognition and grammaticality judgments and were informed of the grammatical nature of the task from the outset, it is unclear whether these activations reflect declarative or nondeclarative memory. Taken together, these studies suggested that the left prefrontal and left occipital cortex were likely to be involved in AGL. However, neither previous study allowed a comparison of

activity evoked by grammatical and nongrammatical stimuli, which can be highly effective in examining nondeclarative memory (e.g., Reber *et al.* 1998a,b).

The current set of experiments attempted to further address the neural underpinnings of AGL by utilizing event-related fMRI. The current design follows the task administration used in studies that have shown AGL to be supported by nondeclarative memory (e.g., Knowlton *et al.*, 1992). The event-related design allowed for a more precise examination of the neural correlates of AGL by allowing an analysis of differential activity for grammatical versus nongrammatical stimuli and an analysis of activity for correct versus incorrect items, in addition to identifying the broader network of brain areas involved in performing the task. Brain areas exhibiting increased activity during successful grammaticality judgments should indicate areas involved in the successful retrieval and application of rule knowledge. The grammatical and nongrammatical stimuli are highly similar except for the fact that the nongrammatical strings contain a deviation from the underlying rule structure (Fig. 1). Thus, additional activity for grammatical strings should identify brain areas responsive to grammaticality. One of the challenges of studying nondeclarative memory in healthy participants is the possibility of the recruitment of declarative strategies during task performance. While successful grammaticality discrimination in patients with MTL damage indicates that these regions are not required for AGL (Knowlton *et al.*, 1992; Knowlton and Squire, 1994, 1996), healthy participants could make judgments based partly on strategies dependent on declarative memory (e.g., recognition of fragments of studied strings). Thus, imaging data were also collected during a matched recognition control condition for comparison to brain activity associated with AGL.

## MATERIALS AND METHODS

### Subjects

The participants consisted of 23 (12 male, 11 female) right-handed volunteers recruited from the Northwestern University community. They were screened for compatibility with the MRI and a history of head trauma and were paid for their participation.

### Stimuli

Grammatical letter strings were generated from a finite-state Markovian rule system (Fig. 1). Twenty-five grammatical study and 25 grammatical test strings were created by traversing the diagram in Fig. 1 from the IN arrow to the OUT arrow, adding a letter at each transition from one state to the next. The resulting study and test strings ranged in length from

3 to 10 letters. Twenty-five nongrammatical test strings were also generated from the same rule system but included a violation in at least one of the state transitions. In the recognition test, the same study items were used in the study phase outside the scanner. During the test, participants were shown the 25 “old” grammatical study items and 25 novel strings (13 grammatical, 12 nongrammatical).

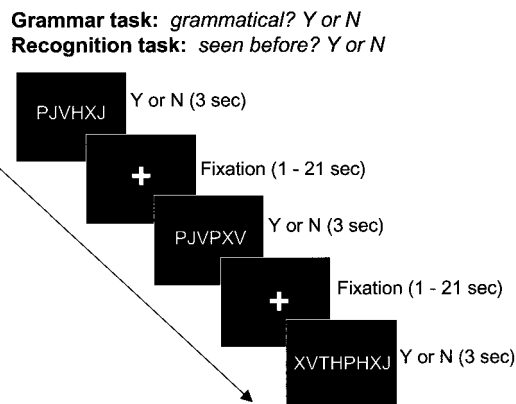
To facilitate the deconvolution of hemodynamic responses from the fMRI data, 50 blank (fixation point) trials were interspersed among the test stimuli to create interstimulus intervals that maximized the separability of evoked responses.

### Procedure

Participants in the AGL and recognition conditions first engaged in a study phase outside the scanner in which they observed 25 grammatical letter strings (one at a time) presented for 3 s each and then attempted to reproduce the string from short-term memory in writing. Participants were given three chances to correctly reproduce each string and if unsuccessful after three attempts, participants copied the string from the study card. The set of 25 study items was presented twice (50 total study trials). After the study phase and just prior to scanning, participants were informed that the items they had just seen were constructed according to a complex set of rules. They were informed that they would enter the scanner and would see new letter strings, some of which followed the rules from the study set, and some which violated the rules. Participants were instructed that if they did not have a clear idea of what the rules were (as expected, since they were not told in advance about the rules and this form of nondeclarative memory typically occurs outside awareness) they should classify these new strings based on their “gut feeling” or instinct. They were told to answer “yes” if they thought the string was grammatical and “no” if it was nongrammatical. Twelve participants engaged in the AGL task (Fig. 2).

A separate group of 11 participants performed a recognition test matched to the AGL procedure. These participants received an identical study phase, but were given a recognition test for these items while fMRI data were collected. During scanning, participants answered “yes” (via a button press on a fiberoptic response box) if they thought they had seen the string in the study phase and “no” (via a separate button on the response box) if they thought it was novel.

All test stimuli were presented for 3 s, and participants made all responses while the stimuli were present. The grammatical and recognition runs administered during scanning were performed twice, and the experiment took approximately 1 h.



**FIG. 2.** Schematic of the grammar, recognition, and encoding tasks. Participants responded “yes” (Y) or “no” (N) with a button press. A fixation point was presented between trials for 1–2 s. The length of the inter-trial interval (ITI) was pseudorandom and based on between zero and five 4-s “fixation-only” trial periods arranged to maximize the separability of the measured hemodynamic response to stimulus trials.

### MRI Scanning Methods

A 1.5 Tesla Siemens VISION scanner was used to collect  $T_2^*$ -weighted echo planar (EPI) images with a matrix size of  $64 \times 64$ , echo time (TE) of 40 ms, flip angle of 85 degrees, and in-plane resolution of  $3.75 \text{ mm} \times 3.75 \text{ mm}$ . Scanning covered the whole brain using twenty-four 6-mm axial (slightly oblique to follow the line connecting the anterior and posterior commissures) slices and a TR of 2.0 s. Two runs of 214 repetitions were collected from each participant in each task (4 initial vol to reach steady state, 200 vol during the test phase, and an additional 10 vol at the end of the scan to collect the residual hemodynamic responses of the final trials). For anatomical localization, a high-resolution 3D FLASH  $T_1$ -weighted three-dimensional sequence was acquired subsequently to functional testing (160, 1-mm axial slices, FOV = 240,  $256 \times 256$  matrix).

### Preprocessing

Images were coregistered through time using a three-dimensional registration algorithm (Cox, 1996). EPI volumes were spatially smoothed with a 7.5-mm full-width half-maximum Gaussian kernel to improve signal-to-noise and accommodate residual anatomical differences across participants. Within each run, voxels were eliminated if the signal magnitude changed  $>10\%$  between two samples (2.0 s) or if their mean signal level was below a threshold defined by the inherent noise in the data acquisition. Finally, all of the runs were transformed (Collins *et al.*, 1994) to conform to the atlas of Talairach and Tournoux (1988) with a final voxel size of  $2.5 \text{ mm}^3$ .

### Data Analysis

The data were analyzed using general linear model analysis that extracted average responses to each trial type (D. Ward, *Deconvolution Analysis of fMRI Time Series Data*, <http://afni.nimh.nih.gov/afni>) and included several control variables (average signal and linear drift estimated individually for each of the two runs, and estimates of corrected motion for each time point to remove signal changes that were correlated with head/brain motion). Differences between trial types were calculated from the differential responses to each event type during the peak of the evoked hemodynamic response (defined as a window 4–8 s after stimulus presentation) and were first estimated for each participant individually. The group data were combined using a random-effects analysis to identify areas in which the differences in activity between trial types were consistent across all participants. Areas of significant activity were those which exhibited a significant change by this random-effects analysis ( $t(11) > 3.85$ ,  $P < 0.001$  uncorrected) in a 500-mm<sup>3</sup> cluster. For the across-experiment analysis (AGL versus recognition), a threshold of  $t(21) > 3.6$  ( $P < 0.001$ , uncorrected) in a 500-mm<sup>3</sup> cluster was used. Monte Carlo simulations using normally distributed noise with 420 time points (equivalent to the two runs) and 12 simulated participants (normally distributed noise matched to the size and shape of the EPI data for each participant and each simulated voxel was matched to the mean and standard deviation of the corresponding measured voxel) were analyzed using identical methods and indicated an expected rate of less than 0.05 false positives (significant clusters) per experiment with this statistical threshold.

## RESULTS

Participants exhibited knowledge of the grammar during the AGL test by successfully discriminating between grammatical and nongrammatical items (57.4% correct,  $\pm 1.9\%$ ,  $t(11) = 3.82$ ,  $P < 0.01$ ). In the fMRI data, increased activity for test items (both grammatical and nongrammatical strings compared to the fixation baseline) was observed throughout the occipital, posterior temporal, parietal, and prefrontal cortical areas during the AGL test (Fig. 3), reflecting the complex nature of the task (visually presented stimuli, decision processes about the stimuli, motor responses, and identifying grammatical strings).

Regarding the grammatical vs nongrammatical strings, increased activity was observed in the left superior occipital gyrus (BA 19) and in the right fusiform gyrus (BA 37) (Fig. 4a, Table 1). The two types of letter strings were highly similar except that the nongrammatical strings contained a deviation from the underlying rule structure (Fig. 1). Thus, the additional ac-

tivity for grammatical strings identifies brain areas responsive to the grammaticality of the test stimuli.

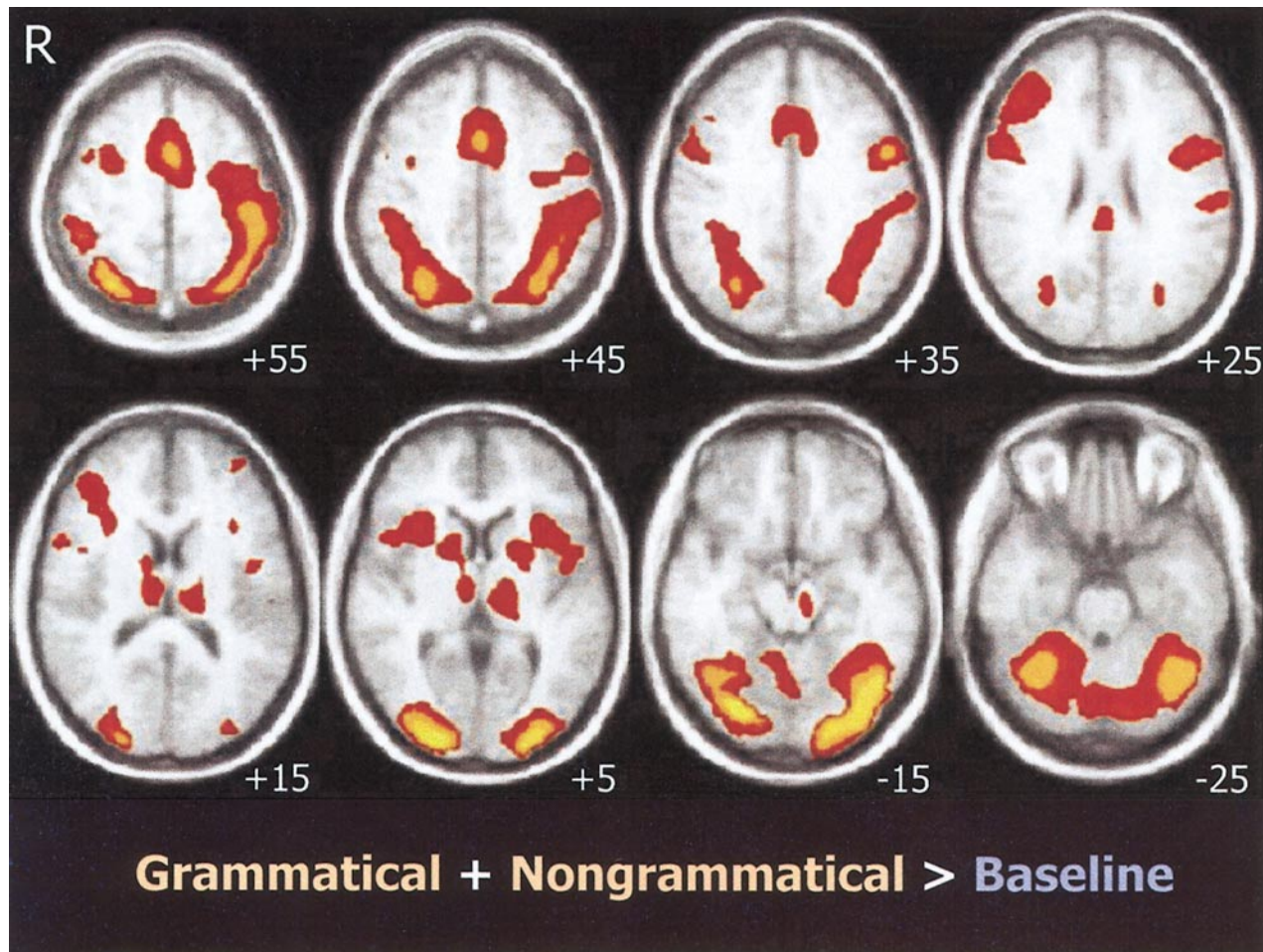
Brain areas involved in the successful application of grammatical knowledge should exhibit increased activity for correct grammatical judgments compared with incorrect judgments (for both grammatical and nongrammatical strings). In comparing correct and incorrect AGL trials, increased activity was observed for successful grammatical judgments in the left superior occipital gyrus (BA 19), the angular gyrus bilaterally (BA 39), the precuneus (BA 7), and the left middle frontal gyrus (BA 6) (Fig. 4b, Table 1). Of particular interest is the selective activation of neighboring areas of the left superior occipital gyrus for grammatical strings and for successful grammatical judgments (circled areas in Figs. 4a and 4b, respectively). Both of these contrasts, which should identify areas involved in the representation and expression of grammar knowledge, identified the left superior occipital gyrus, making this area a prime candidate for the neural substrate of AGL.

No area of differential activity was identified with the comparison between the activity for grammatical and nongrammatical strings for successful compared to unsuccessful judgments. While the interaction between these factors was potentially interesting, the smaller number of trials used in each cell of this analysis reduced the power to observe reliable differences. There may be an area of increased activity for grammatical strings during successful judgments, but the current study did not provide evidence for this.

For the recognition task, participants successfully identified the studied strings, (65.1% correct,  $\pm 2.5\%$ ,  $t(10) = 6.13$ ,  $P < 0.001$ ). The brain areas supporting recognition were compared to the brain areas supporting AGL by contrasting the level of evoked activity during recognition and that evoked during grammaticality judgments (across all stimuli within each condition). One area exhibited greater activity during the AGL task than during recognition in the left angular gyrus (BA 7) (circled area in Fig. 4c, Table 1). This is one of the areas that exhibited increased activity for successful grammaticality performance (Fig. 4b). We identified two areas which exhibited increased activity during recognition judgments (Fig. 4c, Table 1): the left inferior prefrontal cortex (BA 47) and the right anterior cingulate (BA 32). These differences indicate that there are several areas of nonoverlapping brain regions that support the implicit AGL task and the explicit recognition task (particularly the left angular gyrus for AGL).

## DISCUSSION

Across the three contrasts diagnostic of the expression of AGL, two brain areas exhibited consistent increases in activity: the left superior occipital cortex and



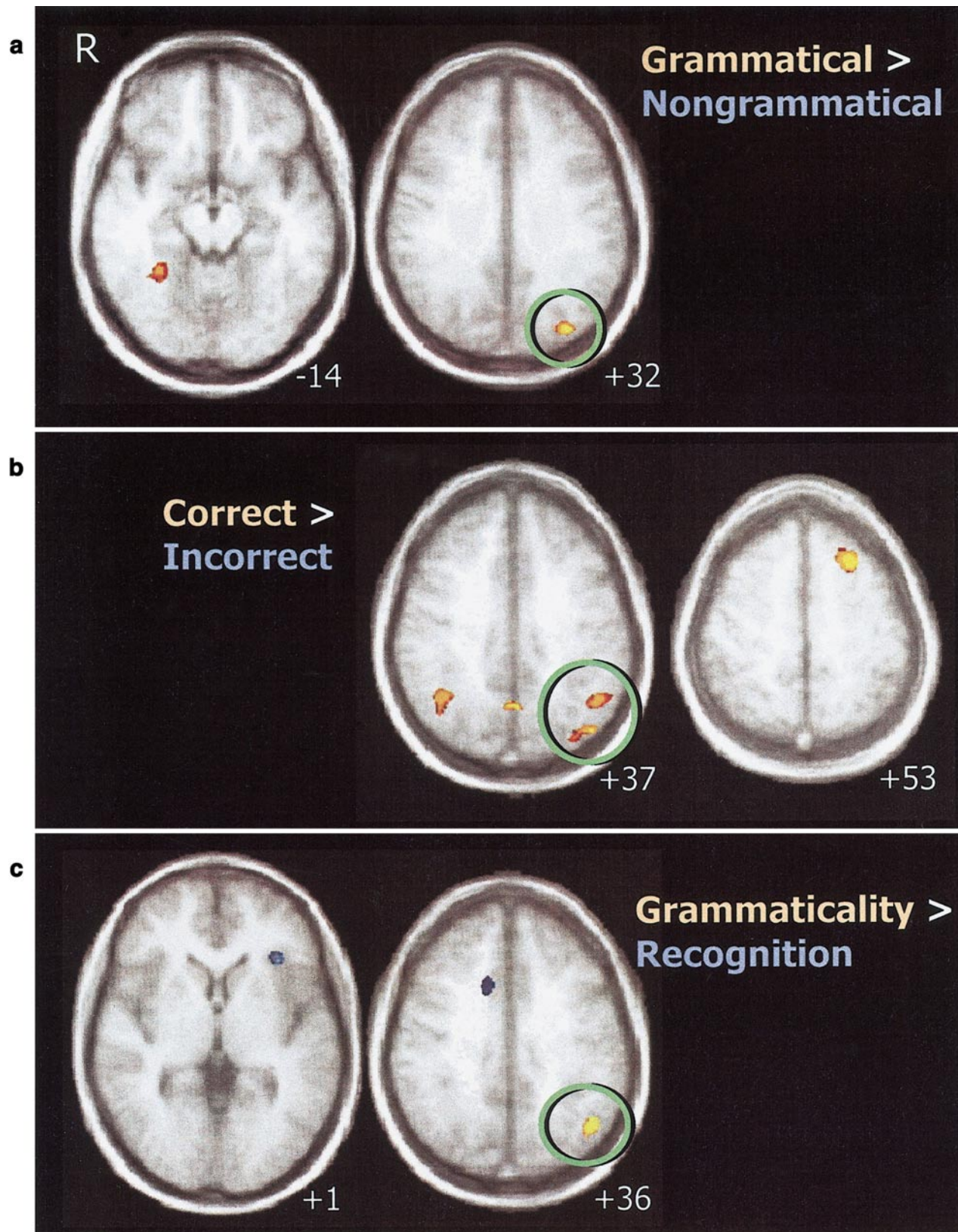
**FIG. 3.** Activity evoked during the grammaticality test for both grammatical and nongrammatical stimuli compared to rest. Areas of activation include widespread occipital, posterior temporal, parietal, dorsolateral, and medial prefrontal cortical areas. All images are oriented according to the radiological convention with the right side of the brain on the left side of the image.

the left angular gyrus. The left superior occipital gyrus was more active for grammatical than for nongrammatical letters strings and was more active for correct judgments of grammaticality during the grammaticality test. The left angular gyrus was also more active during correct judgments and during AGL judgments compared to during recognition judgments. These two areas are therefore prime candidates for the neural substrate of AGL. The hypothesis that these areas of the superior occipital and inferior parietal cortex support AGL is consistent with reports of preserved learning by patients with amnesia (e.g., Knowlton *et al.*, 1992), Parkinson's disease (Reber and Squire, 1999; Peigneaux *et al.*, 1999), and Alzheimer's disease (Reber *et al.*, 2000). Each of these syndromes reflects damage to one or more memory system of the brain (the MTL and/or basal ganglia), yet are not associated with damage to the cortical areas associated with AGL in this report.

It should be noted that although the left superior occipital cortex and left angular gyrus appear to play a critical role in expressing knowledge of an artificial

grammar, these areas must act in concert with other high-order cognitive networks to perform the grammaticality decision task. These areas may also not reflect the complete set of areas involved in the neural substrate of artificial grammar knowledge, as there may be additional areas of activity in individual participants that did not emerge in the group averages (e.g., because the areas did not normalize to the same atlas coordinates).

The brain areas identified as neural correlates of AGL are consistent with several of the areas observed by Seger *et al.* (2000), particularly the left middle frontal and occipital/parietal cortices. Previous results (Seger *et al.*, 2000; Fletcher *et al.*, 1999; Dolan and Fletcher, 1999) have also reported involvement of the left prefrontal cortex during AGL discrimination, which was not found here. While the current lack of observed increased activity in the left prefrontal cortex does not rule out its involvement, the ability to do specific stimulus-based contrasts in the current event-related design and the consistency of AGL-related in-



**FIG. 4.** Areas of evoked activity resulting from contrasts diagnostic of AGL. Warm colors, red–orange–yellow, represent areas of activity for grammatical stimuli (a), correct responses during AGL (b), and the AGL task (c). Cool colors (blue) represent greater activity for the recognition task (c). Areas circled represent areas of activity consistent across contrasts. (a) Grammatical letter strings elicited greater activity in the right fusiform and left lateral occipital gyrus compared to nongrammatical letter strings. (b) Comparing performance on the

**TABLE 1**  
Talairach Coordinates for Areas of Activity across Each Contrast

Brain region	x	y	z	BA
Grammatical–nongrammatical ( <i>G–NG</i> )				
Left superior occipital gyrus	–32	–81	31	19
Right fusiform gyrus	32	–49	–14	37
AGL performance ( <i>correct–incorrect</i> )				
Right angular gyrus	44	–59	37	39
Left middle frontal gyrus	–24	22	53	6/8
Left angular gyrus	–50	–58	35	40
Left superior occipital gyrus	–42	–76	37	19
Precuneus	0	–64	40	7
AGL stimuli versus recognition stimuli ( <i>AGL–Recog</i> )				
Left inferior frontal gyrus deactivation	–33	26	–2	47
Left angular gyrus	–46	–65	38	39
Right anterior cingulate deactivation	13	15	36	32

*Note.* Regions exhibiting changes in activity consisted of clusters of at least 500 mm<sup>3</sup> in which each voxel was consistently active across participants [ $t(11) > 3.85$ ,  $P < 0.001$  uncorrected for the grammatical–nongrammatical and AGL performance contrasts]. For the grammar task–recognition task,  $t(21) > 3.6$  ( $P < 0.001$  uncorrected). Cluster and  $t$  statistic thresholds were identified by Monte Carlo simulation as eliminating false positives  $P < 0.05$  corrected in matched noise data.

creases in activity in posterior areas suggests that these posterior areas are more likely to be specifically involved in AGL. The prefrontal cortex was strongly activated compared with the baseline (visual fixation) but may be playing a more general role in the expression of knowledge (e.g., response selection).

A surprising commonality between the current results and previous neuroimaging studies of memory was evident in the pattern of activity associated with correct grammaticality decisions. Increased activity in the precuneus and bilateral parietal cortex has been reported in several studies of “retrieval success” (Von Zerssen *et al.*, 2001; Konishi *et al.*, 2000) for conscious, declarative memory retrieval. One possible explanation for the activation of a conscious retrieval success network is that there is some contamination from declarative memory retrieval in the current implementation of the nondeclarative memory AGL task (healthy participants are certainly capable of attempting to consciously retrieve information about previously seen stimuli). Another possibility is that this network reflects some more general success monitoring process that is applicable even when information is being retrieved outside awareness from nondeclarative memory. In evaluating these possibilities, it is important to note that a significant difference was found between the recognition and grammaticality tasks, suggesting that different processes (and brain areas) are involved in AGL even if participants attempt some recognition. In addition, participants generally report having to guess at grammaticality, suggesting that it would be

fairly difficult to monitor success (no feedback is given during the test). A third alternative is that although the activity pattern appears similar, the cognitive process expressed in AGL could be different from that expressed during retrieval success conditions in recognition.

One of the goals of examining brain activity specifically associated with AGL is to suggest mechanisms for the cognitive processes that support this type of nondeclarative memory. Previous studies of visual category learning have identified stimulus-correlated activity in the posterior occipital cortex in a nondeclarative memory task (Reber *et al.*, 1998a,b). In those reports, early visual processing areas (BA 17,18) were found to be less active for category members than for nonmembers after learning the category. The reduction in activity observed for novel category members was qualitatively similar to the neural correlates of priming (Buckner *et al.*, 1998), suggesting that these two forms of nondeclarative memory may be supported by similar fluency-based mechanisms. Fluency for grammatical stimuli was not observed in the current AGL study, as there was greater activity for grammatical versus nongrammatical stimuli in the superior occipital cortex (BA 19). Thus, the neural substrate of AGL appears to differ from visual categorization (and priming) in terms of both the localization of memory and the stimulus-correlated activity associated with expressing the memory.

Candidates for cognitive mechanisms in AGL are suggested by similarities between the patterns of ac-

AGL task yielded greater activity in the precuneus, bilateral angular gyri, and left middle frontal gyrus for correct items. (c) In the comparison of the AGL and recognition experiments, AGL evoked greater activity in the left angular gyrus, while recognition lead to greater anterior cingulate and left insular activity.

tivity observed here and the increased activity associated with word-form processing and mental calculation. It has been consistently shown that letter string presentation elicits greater activity in the fusiform gyri and inferior occipital cortices compared to nonletter stimuli (Petersen *et al.*, 1990; Puce *et al.*, 1996; Uchida *et al.*, 1999). Additionally, the angular gyrus has been proposed to act as a word-form area, as it is reported to exhibit more activity for words than nonword stimuli (Menard *et al.*, 1996; Jessen *et al.*, 1999) and has also been implicated in the functional connectivity study of Horwitz *et al.* (1998), which found strong functional linkages between the left angular gyrus and the left superior and lateral occipital cortices for word and pseudoword processing. The phenomenon of AGL could result from the structured grammatical items becoming more "word-like" and thus could recruit similar mechanisms for discriminating between words and nonwords in grammaticality judgments.

In addition to parallels with word-form processing, several neuroimaging studies have demonstrated increased activity in the left angular gyrus in arithmetic calculation tasks (Rueckert, *et al.*, 1996; Menon *et al.*, 2000; Gruber *et al.*, 2001). The structure of the AGL items is evident in the complex patterns among the letters in the stimuli and the ability to acquire and use this information may depend on some of the same cognitive processes involved in mental calculation. Being able to perform AGL may depend on recruiting these cognitive processes for successful grammatical judgments, even when the calculation appears to operate outside awareness (participants are unable to report any calculation processes guiding AGL decisions). This possibility may reflect an alternate mechanism to the learning of word form or there may be some more basic mechanism involved in both of these processes and AGL, e.g., one based on the learning of structured patterns in symbolic stimuli.

Consistent activation in the left superior occipital cortex and left angular gyrus across separate stimulus and task-specific contrasts suggests that these brain areas are involved in AGL. It should be noted that the network of activity observed in the current study likely reflects the *expression* of artificial grammar knowledge, given that only the AGL test phase was subject to functional imaging. Any implicit learning of the rule structure presumably occurs during the study phase, when the grammatical stimuli are first presented. Further work will be necessary to ascertain whether the neural correlates of AGL acquisition resemble the network associated with the expression of grammar knowledge. The occipital/parietal areas that exhibited increased activity for grammatical stimuli bear some resemblance to brain activity-associated word-form processing and mental calculation, suggesting potential mechanisms to be explored. The pattern of increased activity for the rule-conforming grammatical

items suggests that the nondeclarative memory supporting AGL is based on a cortical mechanism different from that which has been suggested to support priming and visual categorization learning (fluent reprocessing). Thus, these findings document a novel nondeclarative memory network supporting AGL.

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