

Language Learning under Working Memory Constraints Correlates with Microstructural Differences in the Ventral Language Pathway

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The present study combined behavioral measures and diffusion tensor imaging to investigate the neuroanatomical basis of language learning in relation to phonological working memory (WM). Participants were exposed to simplified artificial languages under WM constraints. The results underscore the role of the rehearsal subcomponent of WM in successful speech segmentation and rule learning. Moreover, when rehearsal was blocked task performance was correlated to the white matter microstructure of the left ventral pathway connecting frontal and temporal language-related cortical areas through the extreme/external capsule. This ventral pathway may therefore play an important additional role in language learning when the main dorsal pathway-dependent rehearsal mechanisms are not available.

Keywords: DTI, extreme capsule, language learning, ventral pathway, working memory

Introduction

Increased knowledge about the cognitive mechanisms and neural substrates that allow humans to learn language is essential to understand individual differences in the acquisition of first and second languages. Individual differences in working memory (WM) may modulate language learning abilities (see Service 1992 for children; Ellis and Sinclair 1996 and Papagno and Vallar 1995 for adults; and Freedman and Martin 2001 for patients with short-term memory deficits).

Following Baddeley's model (Baddeley and Hitch 1974; Baddeley 2003b), the phonological loop component of WM (pWM) is involved in the temporary maintenance and manipulation of verbal information. The pWM is further divided into 2 subcomponents: the limited capacity "phonological store" retains verbal and acoustic information, whereas the "articulatory rehearsal" through a subvocalization mechanism maintains the information active in the store for a longer period of time to allow retrieval and/or manipulation.

Neuroanatomically, the pWM network and brain regions devoted to speech perception and production have been shown to overlap (Jacquemot and Scott 2006). The phonological store has been mainly associated with the left inferior parietal cortex (Broca's area [BA] 40) (Jonides et al. 1998; Smith and Jonides 1998; Ravizza et al. 2004; Baldo and Dronkers 2006), whereas the articulatory rehearsal has been linked to the left ventrolateral prefrontal cortex (BA 44/45), left pre-

SMA, left premotor cortex (BA 6), and right cerebellar cortex (Paulesu et al. 1993; Chein et al. 2003; Chen and Desmond 2005a, 2005b). The role of rehearsal, reflected in left premotor activation, has been evidenced in early stages of segmentation of an artificial language, word learning (McNealy et al. 2006; Cunillera et al. 2009) and grammar acquisition (Opitz and Friederici 2004; for behavioral studies, see Williams and Lovatt 2003; Ellis 2006; Kempe et al. 2009).

The frontoparietal areas required for those functions are connected by 2 alternative pathways. Dorsally, the posterior superior temporal lobe (STL) is directly connected to BA 44/45 and to the premotor cortex via the long segment of the arcuate fasciculus (AF) and the superior longitudinal fasciculus (SLF). The frontal and the temporal lobes are also connected indirectly by an anterior segment connecting the frontal and inferior parietal lobes and a posterior segment connecting the parietal and temporal regions (Catani et al. 2005). Those connections are involved—among other functions—in the mapping of phonemic to motor representations through articulation required for language production and rehearsal (Anderson 1999; Wise et al. 1999; Hickok and Poeppel 2004; Hickok and Poeppel 2007).

Children between 2 and 4 years of age are already able to perform nonword repetition tasks that involve rehearsal (Roy and Chiat 2004), although this component may not be fully developed before age 7 (Gathercole et al. 1994; Baddeley et al. 1998; Gathercole 1999; Gathercole et al. 2004; Roy and Chiat 2004). Accordingly, although the dorsal pathway connecting the frontoparietal network sustaining pWM is still under development at this age (Dubois et al. 2008; Brauer et al. 2011), children are still able to acquire most language properties before its complete maturity. Therefore, either their phonological store is sufficient to allow initial learning or there is an alternative mechanism to maintain the information in an active state (Gathercole et al. 1994). This raises the question of which neural pathway is engaged when the dorsal pathway is not completely available or fully developed.

In this sense, an alternative ventral route through the extreme capsule (EmC) has been recently proposed to connect the middle section of the STL with the frontal operculum (FOP) (BA 45) close to the insular cortex (Makris and Pandya 2009). In the first diffusion tensor imaging (DTI) on the asymmetry of the AF, Parker et al. (2005) already noted that, in some participants, an additional more ventral pathway existed

connecting the superior temporal cortex with inferior frontal regions (see Croxson et al. 2005 and Anwander et al. 2007). This pathway has been implicated in language comprehension (Saur et al. 2008; Friederici 2009) and in the top-down regulation of linguistic processing that is involved in verbal retrieval (see also Petrides and Pandya 2006; Frey et al. 2008) but its specific role is still controversial. Recently, Saur et al. (2008) have linked this ventral connection to the monitoring required during word repetition, suggesting a functional connection to the rehearsal mechanisms of pWM. The EmC pathway is different from the more ventral route, the inferior fronto-occipital fasciculus (IFOF) that has been associated with semantic processing (Duffau et al. 2005).

Because earlier work has focused on the acquisition of vocabulary (Gaulin and Campbell 1994; Gathercole et al. 1997; Baddeley et al. 1998; Baddeley 2003a; Gathercole 2006), less is known about the role of pWM in speech segmentation and rule learning, which are important processes for language learning (Rodríguez-Fornells et al. 2009). The segmentation process is not obvious because the speech signal is mostly uttered as a continuous string of sounds, and there are no reliable acoustic cues indicating word boundaries. To solve this problem, the learner needs to keep track of sequential information in the stimulus stream, by exploiting different acoustical (i.e., allophonic variation, stress patterns, and prosody) and distributional cues (i.e., phonotactic regularities and transitional probabilities of syllable combinations) (Jusczyk 1999). In a later stage, the learner must advance from detecting simple and adjacent relationships to detecting more abstract and non-adjacent relationships, such as subject-verb agreement, to derive morphosyntactic rules of the language (e.g., “*he reads*,” “*he plays*,” “*he jumps*”).

The aim of the present study was to determine whether the phonological store and articulatory rehearsal subcomponents of pWM are essential for segmentation and rule learning and what specific white matter pathways are related to individual differences when the different pWM subcomponents are not available. To study the relationship between pWM and speech segmentation, artificial languages were presented, in which word boundaries had to be learned based exclusively on transitional probabilities between syllables (Saffran et al. 1996; Cunillera et al. 2006). To study the relation between pWM and rule learning, in another condition, words were presegmented by subtle pauses but contained embedded rules that had to be extracted (Peña et al. 2002; De Diego-Balaguer et al. 2007). Learning was assessed using 2 WM interference conditions: the articulatory suppression (AS) condition (i.e., blocking the use of rehearsal) and the irrelevant speech (IS) condition (i.e., introducing irrelevant information into the store).

In addition, we adopted a voxel-based whole-brain level linear regression approach to evaluate whether individual differences in language learning performance were correlated with differences in white matter microstructure (defined by fractional anisotropy [FA] values derived from diffusion tensor images; Le Bihan 2006). DTI is sensitive to microstructural differences in white matter because it reflects diffusion of water molecules along certain anisotropic (i.e., preferential) directions (e.g., following axon membranes and myelin sheaths) (Le Bihan 2006). Because the main orientation of water molecules is aligned with the direction of the dominant axonal fibers, this technique allows assess the microstructure of the fibers connecting different brain regions. It has been

shown that individual differences in cognitive tasks can be partially explained by microstructural variations in white matter connectivity between specific brain areas (Audoin et al. 2007; Boorman et al. 2007; Gold et al. 2007; Sepulcre et al. 2008; Charlton et al. 2010; Fuentemilla et al. 2009; Camara et al. 2010; Fleming et al. 2010), as a result of extensive learning (Bengtsson et al. 2005; Scholz et al. 2009) or developmental maturation (Brauer et al. 2011) (for a recent review, see Johansen-Berg 2010). Thus, DTI could show whether individual differences in language learning under WM constraints are related to differences in the white matter properties of particular brain pathways.

Materials and Methods

Participants

Seventy-two native Spanish speakers with no history of neurological or auditory problems (mean age, 22.1 ± 3.8 (standard deviation, SD), 52 women) participated in the behavioral experiment. Each participant was randomly assigned to 1 of the 2 language conditions (segmentation [$n = 35$] or rule learning [$n = 37$]). From those, 44 volunteers (mean age, 21 ± 3.2 (SD), 29 women) also participated in the DTI experiment (segmentation condition [21] and rule-learning condition [23]). The scanning session took place first, and then we added 28 more participants for the behavioral experiment. One hundred thirty-two new volunteers participated in 2 additional control experiments (see Supplementary Results).

Materials and Procedure

The behavioral experiment comprised a “learning phase” during which participants listened to 2 min of an artificial language stream followed by a “test phase” during which a 2-alternative forced-choice (2AFC) task was used to test language acquisition. Previous work has shown that 2 min of exposure was sufficient to extract words (Saffran et al. 1996; Cunillera et al. 2006) and rules (Peña et al. 2002; De Diego-Balaguer et al. 2007) during this type of task. Figure 1 illustrates the behavioral design.

Each participant underwent 2 learning sessions (and their corresponding test phase) using 2 WM conditions: AS and IS. The presentation order of the 2 WM conditions was counterbalanced across participants. During the learning phases, participants were told that they would hear a nonsense language and that their task was to listen attentively because they would be asked to recognize words from this language afterward. In the subsequent 2AFC test, participants were presented with pairs of words, and they were asked to press either the “1” or the “2” key on a keyboard following the presentation of each pair to indicate whether the first or the second word of the pair was a word from the language presented during the learning phase. Test trials were presented in random order. The order of the presentation of the test items in the pair was counterbalanced for each subject. All participants were tested individually while seated in front of a 15” screen in a sound-attenuated room. Instructions were presented on the screen during the experiment.

Language Conditions

Two different 2-min language streams were created for each language condition (segmentation and rule learning) using the text-to-speech synthesizer MBROLA with a Spanish male diphone database at 16 kHz (Dutoit et al. 1996). Each stream was made by concatenating the trisyllabic nonsense words of each language in pseudorandom order with the constraint that a word was never immediately repeated in the stream. All words of the artificial languages respected Spanish phonotactics.

This design enabled us to focus exclusively on the statistical structure of the language and to eliminate other potential segmentation cues, such as word-stress or coarticulation. All phonemes had the same duration (116 ms) and pitch (200 Hz; equal pitch rise and fall, with the

pitch maximum at 50% of the phoneme) in the language streams, with a resulting word duration of 696 ms. Different syllables were used across languages. Words were combined such that each word had an equal probability to be followed by any other word used in the stream. Volunteers were not given information about the structure or length of the words or the number of words composing the language.

Word Segmentation Condition

Language streams followed the structure of those in previous studies (Saffran et al. 1996; Cunillera et al. 2006). Each language was composed of 6 trisyllabic words. The synthesizer did not insert acoustic word boundary cues and produced equivalent levels of coarticulation between all syllables. Thus, the only reliable cue for word boundaries in all streams was the transitional probability of the syllables. Transitional probability was 1.0 for the syllables forming a word and 0.2 for syllables spanning word boundaries. Test items were created to test the participants' segmentation ability. In addition to the 6 words from the learning phase, 36 part-words were created for each language. Half of the part-words were built by combining the final syllable of one word and the first 2 syllables of another word. The remaining part-words were built by combining the last 2 syllables of one word and the first syllable of another word (see Table 1). In a 2AFC test, words and part-words were exhaustively combined, resulting in a total of 36 pairs that were presented randomly over loudspeakers. Presentation of the items of a pair was separated by 500 ms.

Rule-Learning Condition

Language streams were created following the structure of Peña et al. (2002). Each language comprised 9 words, which were built following the rule that a word's initial syllable determined its ending (e.g., **lekadi**, **lefidi**, **lerodi**) irrespective of the middle element. This structure is similar to some morphological rules (e.g., **unbelievable**, **untreatable**, **unbearable**). Three rules were created for each language (see Table 1). We used this type of stream because it ensured a close match with the segmentation task. Moreover, previous work has shown that participants can learn abstract information with these streams, leading

to categorization and transfer to novel material (Endress and Bonatti 2007; De Diego-Balaguer et al. 2008). Consistent with Peña et al. (2002), language streams were presegmented by 25 ms pauses to induce generalizations of structural information. No additional prosodic or acoustical information was available. The transitional probability between the initial and middle syllable or between the middle and final syllable was 0.33. The transitional probability between the first and last syllable of each word was 1.0, whereas the transitional probability between the last syllable of any word and the first syllable of the following word was 0.5. To assess rule-learning abilities in the test phase, 9 nonwords and 9 rule-words were created for each language. Nonwords were composed of the same 3 syllables as words but with the syllables corresponding to the structural rule in an inverted order (see Table 1). In contrast, rule-words were created with the same initial and final syllables of words but with a syllable corresponding to another word inserted in the middle position. Therefore, even though the new words followed the structure of words in the artificial language, the participants had never heard them before. This approach enabled us to test for generalization of the learned rule. The test phase consisted of a 2AFC formed by 18 trials where each test item was repeated twice. Each item pair consisted of a nonword and a rule-word that were separated by 700 ms.

WM Conditions

IS Condition

In this condition, the phonological store subcomponent of PWM was saturated by introducing irrelevant material. Before the beginning of the learning session, we used a digital voice recorder to record participants' voices uttering the syllable "bla" continuously (Besner et al. 1981) for 2 min with homogeneous frequency and volume (average uttering pace was 122.2 ± 17.4 syllables per minute). Both the artificial language to be learned and the prerecorded voice streams were presented through 4 loudspeakers (2 for the language streams and 2 for the IS). The loudspeakers were located symmetrically at an

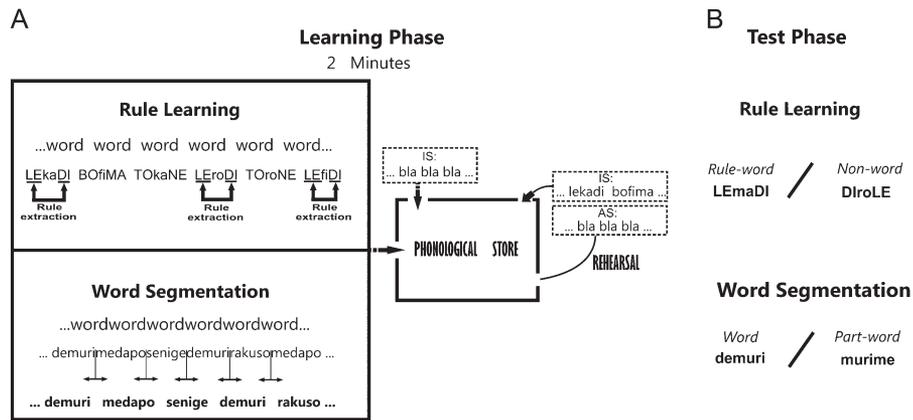


Figure 1. Schematic illustration of the design of the behavioral study. (A) Structure of the 2 types of languages used to induce rule learning and word segmentation. The diagram illustrates the phonological WM components and how, in the AS condition, rehearsal is not available, as participants were required to repeatedly utter the syllable "bla." In the IS condition, rehearsal is free to be used in order to refresh the relevant information, but IS interferes with the phonological store. (B) Structure of the test items for each condition. WM: working memory; IS: irrelevant speech; AS: articulatory suppression

Table 1

Materials used for the segmentation and rule-learning conditions in the behavioral experiment

	Words	Nonwords	Rule-words
Segmentation condition (Language 1)	demuri senige medapo rakuso kotusa lirepu	murise riseni	—
Segmentation condition (Language 2)	pabela dubipe lufagi tagofu rutega kifobu	beladu ladubi	—
Rule-learning condition (Language 1)	lekadi bokama tokane lefidi bofima tofine lerodi boroma torone	dirole	lemadi
Rule-learning condition (Language 2)	bafegu dofeke mofeti bapigu dopike mopiti balogu doloke moloti	gupiba	badogu

Note: All the words used for each language are listed. Examples of test items are provided. In the segmentation condition, nonwords were formed by combining the syllables composing the words (ABC) in 2 ways: BCA or CAB. In the rule-learning condition, nonwords (CXA) were created by inverting the order of each of the rules presented in the language stream (AXC). Rule-words (AXC) are new words following the same structure presented in words from the language stream. "—": not applicable.

angle of 45° and a distance of approximately 30 cm on each side of the subject; speakers were played at equal volume. The 4 loudspeakers were located side-by-side in pairs in such a way that both relevant and IS was heard from loudspeakers on the left and right side of the subject. Participants were informed that they would hear their own previously recorded voice while they were listening to an artificial language stream. They were asked to pay attention to the nonsense language stream and to ignore the irrelevant voice stream.

AS Condition

This condition involved an AS task that interfered with the use of the rehearsal mechanism. Participants had to continuously utter the syllable bla while listening to the language stream (The rehearsal process also allows the manipulation of information held in WM. A manipulation task is thus often introduced along with the AS condition [e.g., a subtraction counting task]. However, this involves the introduction of a dual task that taxes executive function [calculation]. Our intention here was to block only the articulatory component while performing a rather automatic task. For this reason, participants were simply required to repeatedly utter a single syllable.) (Baddeley et al. 1984). The language streams were presented through the same 2 loudspeakers used for the language stream in the IS condition.

DTI Acquisition

DTI data were collected using a 3-T magnetic resonance imaging scanner (Siemens Magnetom Trio) using an 8-channel phased-array head coil with parallel imaging (GRAPPA) and an acceleration factor of 2. Diffusion weighting was conducted using the standard twice refocused spin echo sequence. Images were measured using 2-mm-thick slices (no gap, time repetition = 8200 ms, time echo = 85 ms, 128 × 128 acquisition matrix, field of view 256 × 256 mm, 64 axial slices). To obtain diffusion tensors, diffusion was measured along one nondiffusion-weighted image ($b = 0$ s/mm²) and 12 noncollinear directions (b value of 1000 s/mm²), chosen according to the standard Siemens DTI acquisition scheme. Two signal averages and 3 runs were acquired per slice and per diffusion gradient direction.

Diffusion-Weighted Data Preprocessing

DTI data were corrected for motion prior to estimation of diffusion tensors. The first nondiffusion-weighted image of each block was realigned with the first image of the first series. Then, the determined transformation parameters were applied to the remaining diffusion-weighted images of the block. Subsequently, all images were averaged across the 3 runs. FA values were calculated using the SPM2 diffusion toolbox (<http://www.fil.ion.ucl.ac.uk/spm/>). Diffusion tensor elements were extracted from an overdetermined set of diffusion-weighted images. Diffusion tensors were then diagonalized and eigenvectors and eigenvalues were obtained. Based on these eigenvalues, FA was calculated on a voxelwise basis.

Normalization of FA data was performed based on FA anisotropy images without Jacobian modulation of signal intensities (Camara et al. 2007). Specifically, FA images were first normalized using the echoplanar image-derived Montreal Neurological Institute (MNI) template (ICBM 152) provided by SPM2. From these normalized data sets, a preliminary template was created by signal averaging. Next, FA images were normalized again using this template. Subsequently, a second and final template was created by averaging these newly normalized images after the extraction of only brain parenchyma. The extraction of brain tissue was performed using a 3-class brain tissue segmentation (gray matter, white matter, and cerebral spinal fluid). Individual native-space brain parenchyma maps were extracted from the initial FA images and normalized to the final extracted-brain template. Finally, all individually normalized FA images were smoothed by convolving them with isotropic 8-mm full-width at half-maximum Gaussian kernels.

Diffusion-Weighted Data Analysis

The voxelwise analysis aimed to detect the voxels in which FA values (ranging from 0 to 1) correlated with the 2 learning conditions (IS and AS). Larger FA values indicate that water diffusion occurs preferentially

along one direction, as is the case for the structural organization of white matter tracts (Le Bihan 2003). By applying a simple regression model in SPM2, previously normalized FA images were independently regressed on the proportion of correct responses in AS and IS conditions (independently for segmentation and rule-learning tasks and pooled together for both conditions). This analysis was constrained to those voxels with FA values > 0.15 in each participant. This cutoff allowed us to reliably isolate white matter (Jones et al. 1999). Locations and significance levels from the correlation analysis were restricted to 4 different uncorrected thresholds: $P < 0.05$, $P < 0.01$, $P < 0.005$, and $P < 0.001$ (all of which with a 60-voxel spatial extent) for display purposes (see Figs 3 and 4). The use of this gradual threshold allows the visualization of the underlying white matter path. Significant regions for the whole-brain analysis ($P < 0.001$ and $P < 0.01$, uncorrected) are reported and discussed in the text only when significant (corrected at cluster level, $P < 0.05$) for multiple comparisons. The maximum of suprathreshold regions were labeled following different white matter DTI brain atlas (Wakana et al. 2004; Catani and Thiebaut de Schotten 2008; Thiebaut de Schotten et al. 2011).

Results

Behavioral Results

All the statistical results reported in the present study were replicated when conducted with arcsine transformed data ($\arcsin(\sqrt{\text{percent data}/100})$). Untransformed percentages of correct responses are kept for a clearer description of the results and for display purposes in the figures. Effect sizes are also provided for all statistical analyses. In both AS and IS conditions, the mean percentage of correct responses was significantly above chance (set at 50%) (segmentation condition AS: $t_{34} = 2$, $P < 0.05$ and IS: $t_{34} = 5.4$, $P < 0.0001$; rule-learning condition AS: $t_{36} = 2.3$, $P < 0.05$ and IS: $t_{36} = 3.9$, $P < 0.0001$) (see Fig. 2). Percentages of correct responses for each condition are provided in Table 2. Nevertheless, a repeated-measures analysis of variance, with WM condition (AS/IS) as the within-subject factor and language condition (segmentation/rule learning) as the between-subject factor, revealed a significant main effect of WM condition ($F_{1,70} = 5.43$, $P < 0.05$, $\eta p^2 = 0.07$). There was impaired learning in the AS condition when compared with the IS condition ($54.8 \pm 13\%$ vs. $59.6 \pm 12\%$, respectively) ($t_1 = 2.3$, $P < 0.05$, $d = 0.37$). Neither the language condition effect nor the interactions were found to be significant (all $F < 1$).

Two follow-up control experiments (see Supplementary Results and Fig. S1) showed that whereas the interference with the phonological store did not produce an impairment compared with a condition without interference, the AS condition did impair learning compared with no interference. The between-subjects design of this last experiment corroborated that this effect could not be due to carryover effects between conditions.

DTI Correlations

As no differences were obtained behaviorally in the WM effects for segmentation and rule learning, FA values were correlated with performance in the AS condition pooling together segmentation and rule-learning conditions. However, specific independent correlations for segmentation and rule learning are also provided in the Supplementary Results and Figure S2. In the whole-brain analysis ($P < 0.001$, uncorrected), the overall performance in the AS condition was significantly correlated with FA in the left EmC/external capsule (EC) (MNI peak coordinates (x, y, z): $-27, 9, 0$; t value = 4.35 , $P < 0.05$, corrected

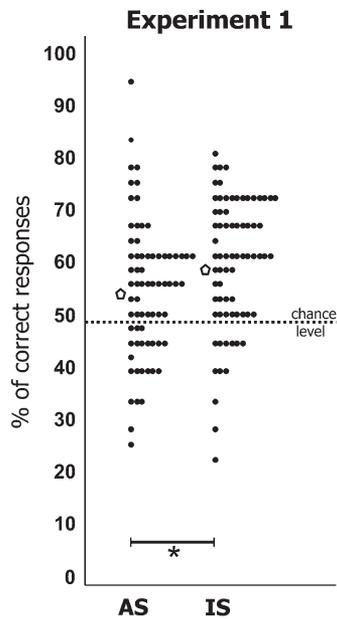


Figure 2. Distributions of the percentages of correct responses (for segmentation and rule learning together) in the 2 alternatives forced-choice test for Experiment 1. This test was administered after each language exposure in the IS and AS conditions. * $P < 0.01$. Each point corresponds to an individual participant score, and pentagons denote the group mean for each condition. AS: articulatory suppression; IS: irrelevant speech.

Table 2
Mean percentages of correct responses and standard error of the mean in Experiment 1

	Experiment 1	
	AS	IS
Segmentation	53.9 (2.2)	60.2 (2.1)
Rule learning	55.5 (2.2)	59.3 (2.1)

at cluster level, 60-voxel spatial extent (see Fig. 3)) when segmentation and rule-learning conditions were collapsed. No significant FA correlations were obtained for the IS condition at this threshold. Nevertheless, at lower thresholds ($P < 0.01$, uncorrected), a spatially distinct correlation pattern was seen for the IS condition. In this case, the ventral part of left anterior-posterior directed fibers, in particular the anterior branch of the cingulum which runs medially close to the corpus callosum, was identified (MNI peak coordinates (X, Y, Z): $-29, 32, 8$; t value = 2.42 , $P < 0.05$ corrected at cluster level, 60-voxel spatial extent (see Fig. 4)) (Wakana et al. 2004; Catani and Thiebaut de Schotten 2008; Thiebaut de Schotten et al. 2011).

Discussion

In the present investigation, we combined behavioral manipulations and DTI data to study the role of pWM in segmentation and rule learning. Individual differences in language learning under rehearsal blockage were related to left hemisphere white matter microstructural differences between the putamen and the insular cortex corresponding to the location of the fiber bundles running through the EmC/EC. In addition, behavioral results support a role for the articulatory rehearsal subcomponent of the phonological loop in language acquisition.

WM Differences in Language Acquisition

By blocking rehearsal, segmentation and rule learning were significantly impaired when compared with a language learning condition with no interference (Supplementary Results and Fig. S1) or to conditions interfering with the phonological store (see Table 2 and Fig. 2). Importantly, although the speech segmentation and the extraction and generalization of non-adjacent dependencies have been proposed to require different computational mechanisms (Peña et al. 2002), our results suggest a similar contribution of pWM to the learning of both types of information.

The capacity of the phonological store has been previously correlated with the learning of new vocabulary (Papagno et al. 1991; Service 1992; Papagno and Vallar 1995; Gathercole et al. 1997; Baddeley et al. 1998; Gathercole et al. 2003). Thus, the phonological store was deemed necessary for new vocabulary learning (see also Freedman and Martin 2001), whereas articulatory rehearsal was viewed as a simple promoter mechanism, especially in adult second language learning. While previous studies have reported an association between phonological short-term memory and grammar learning, they did not investigate the contributions of different WM sub-components (Williams and Lovatt 2003; Kempe et al. 2009). Similarly, Ellis and Sinclair (1996), using an AS task, found a strong relationship between syntactic learning and the rehearsal component of pWM, but they included semantic information and no exploration about the phonological store was done. Consequently, to our knowledge, this study is the first that has directly evaluated the specific role that the rehearsal and the phonological store play in 2 key aspects of language acquisition, when no semantic information is available (Rodríguez-Fornells et al. 2009).

Individual Differences in White Matter Pathways Related to Articulatory Rehearsal in Both Language Learning Conditions

Individual differences in white matter microstructure were related to learning variability under AS conditions. Specifically, left lateralized fiber bundles running between the putamen and the insula via the EmC/EC were correlated with performance. These bundles are part of an alternative pathway (i.e., a ventral pathway) to the classic dorsal language pathway (AF, SLF), which has been associated with phonological and articulatory processes.

The EmC contains several white matter fiber tracts connecting the FOP to the STL. One tract connects the FOP to the mid portion of the STL, anterior to Heschl's gyrus, and the other involves the uncinate fascicle (UF) and connects the FOP and the lateral orbitofrontal cortex to the anterior temporal lobe (Friederici 2009). This latter tract enters the EC and contributes fibers to the inferior fronto-occipital fasciculus (Catani and Mesulam 2008; Fernandez-Miranda et al. 2008). Although several studies have been able to dissociate the EmC and nearby EC fiber systems (Catani and Mesulam 2008; Makris and Pandya 2009), the current methodology approach is limited in the ability to distinguish pathways running in close proximity (Frey et al. 2008; Friederici 2009). However, based on monkey anatomical tracer studies, it has been shown that the connection between the superior temporal gyrus and the ventrolateral prefrontal region (which is the homolog of BA 45 in humans)

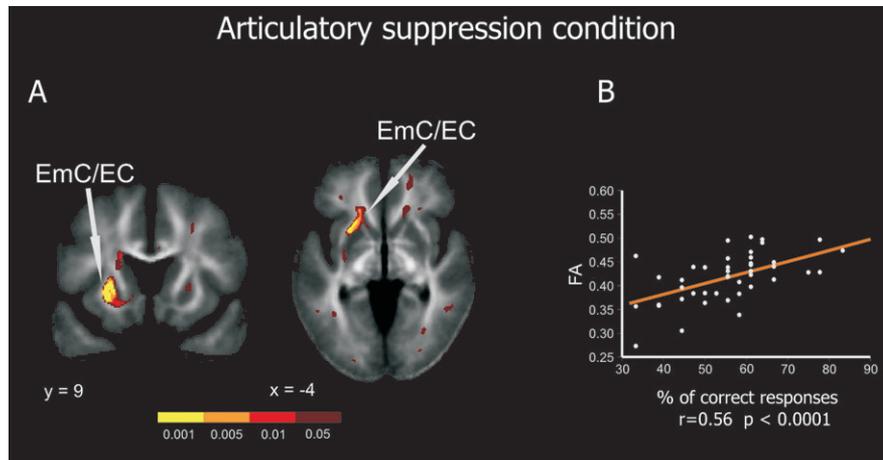


Figure 3. Individual differences in segmentation and rule-learning conditions with AS correlated with FA of major white matter tracts. (A) Significant white matter–correlated clusters ($P < 0.001$; $n = 60$ voxels) rendered on the FA mean image in a coronal (left) and transverse (right) view. The same results are shown with a more liberal statistical threshold to visualize the white matter pathways, $P < 0.005$; $P < 0.01$; $P < 0.05$; $n = 60$. (B) Relationship between the mean FA value for each participant at the peak of the correlated region of interest and the performance in the AS condition for segmentation and rule learning (left EmC, peak MNI coordinates $x = -27$, $y = 9$, $z = 0$). Color bar indicates the P values. EmC: extreme capsule; EC: external capsule.

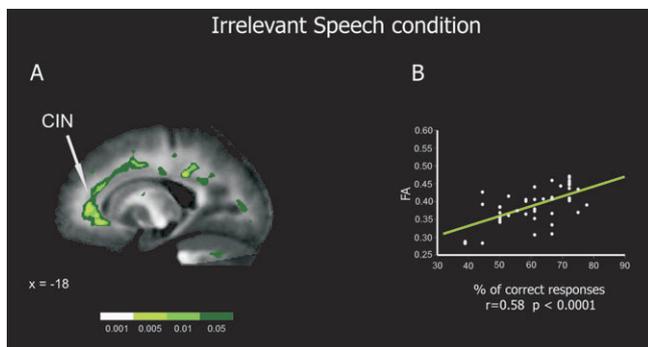


Figure 4. Individual differences in segmentation and rule learning under the IS condition correlated with FA of major white matter tracts. (A) Significant white matter correlated clusters ($P < 0.01$; $n = 60$ voxels) are rendered on the FA mean image. The same results are shown with a more liberal statistical threshold to visualize the white matter pathways, $P < 0.005$; $P < 0.01$; $P < 0.05$; $n = 60$. (B) Relationship between mean FA value for each participant at the peak of the correlated region of interest and the performance in the IS condition (left anterior cingulum, peak MNI coordinates $x = -29$, $y = 32$, $z = 8$). Color bar indicates the P values. CIN: cingulum.

occurs via a pathway through the EmC (Petrides and Pandya 2009).

Although the ventral EmC pathway has been mainly associated with language comprehension (Saur et al. 2008), it has been recently proposed as an alternative route for phonological processing in addition to the dorsal pathway (Saur et al. 2010; Brauer et al. 2011). Interestingly, the ventral pathway appears to be more prominently used for language processing during childhood than in adulthood due to its early development even in tasks that normally (i.e., in adults) require the dorsal pathway (Brauer et al. 2011). In this vein, Saur et al. (2008, 2010) have linked the ventral pathway to rehearsal mechanisms, a function which is classically associated to the dorsal pathway. Individual differences in the execution of a WM-dependent task have also been linked to the ventral EmC pathway (Charlton et al. 2009), and this path has been proposed to have a role in serial processing of

representations at different levels (i.e., segments, syllabic structure, phonological word forms, grammatical features, and semantic information).

How can the current results be interpreted in light of this evidence? Behavioral results showed that language learning was dependent on the articulatory rehearsal mechanism, and DTI correlations suggested that participants with a more evolved ventral EmC pathway show better performance because they can recruit this pathway to a greater extent for language learning. Therefore, although the functional role of this pathway is still under debate (Friederici 2009), a growing body of literature suggests its important role in linguistic-related functions (Frey et al. 2008; Makris and Pandya 2009; Petrides and Pandya 2009). In this sense, our study provides support to the idea that this ventral EmC pathway may be recruited along with the dorsal pathway during development or under high load conditions (as in the AS learning task) as an alternative maintenance mechanism (Saur et al. 2010; Brauer et al. 2011).

This functional role would be consistent with the use of the EmC ventral pathway in infancy when the dorsal pathway is still under development (Giorgio et al. 2008; Brauer et al. 2011), and when the rehearsal mechanism of WM that may rely on the dorsal pathway is not yet fully available (Gathercole et al. 1994; Baddeley et al. 1998; Gathercole 1999). Moreover, recruitment of this ventral pathway attests to the high flexibility of the learning system when the dorsal pathway is saturated by a secondary task during learning. This idea of a supplementary mechanism is consistent with recent data on patients with temporal lobe resections that indicate that an increased FA postoperation in this ventral path is predictive of a better language outcome after surgery (Yogarajah et al. 2010). Nevertheless, the specific nature of the additional functions supported by this path (e.g., executive functions, WM subprocesses) cannot be determined with the current data.

Because of the limitations of the current DTI methodology in differentiating the EC and the EmC pathways, it is important to mention also the possible involvement of fibers from the UF, which enter the EC and that also contribute to the IFOF (Catani and Thiebaut de Schotten 2008). The UF has been linked to

local phrase structure building (Friederici et al. 2006; Friederici 2009) in artificial language learning tasks devoid of semantic information. However, a recent intraoperative electrical stimulation study showed no direct effects of the stimulation of the UF pathway on language processing or residual language deficits after the resection of at least part of the UF (Duffau et al. 2009). In addition, the IFOF has been implicated in semantic processing because direct electrical intracortical stimulation elicits semantic paraphasias (Duffau et al. 2005; Duffau 2008). Thus, because these pathways, particularly the IFOF, have been implicated in higher level comprehension processes, we believe that involvement of these pathways in articulatory rehearsal is less plausible than the EmC pathway discussed above.

Finally, in addition to these anterior–posterior tracts, the EC receives corticostriatal projection fibers. Although the pathway identified in our study, which extends to the flank of the medial wall of the insula, is in line with the EmC anterior–posterior fiber pathway trajectory (see Fig. 3), a more simplified explanation related to the residual articulatory capacity should be considered. Thus, the microstructural differences obtained in our study could be related to these corticostriatal projection fibers that convey information from several frontal cortical areas (i.e., ventrolateral prefrontal cortex [BA 44/45], left pre-SMA, and left premotor cortex [BA 6]) through the EC to the putamen, caudate nucleus, and claustrum (Lehericy et al. 2004; Leh et al. 2007; Fernandez-Miranda et al. 2008). This interpretation would be in agreement with the role of the putamen in speech production (Wise et al. 1991; Duffau et al. 2005) and speech-based rehearsal (Awh et al. 1995; Logie et al. 2003; Chang et al. 2007).

Conclusions

The current study produced 2 main findings. First, the articulatory rehearsal subcomponent of the phonological loop involved in WM plays an important role in segmentation and rule learning. Second, individual differences in language learning in the AS task could be attributed, at least in part, to individual differences in the white matter fiber bundles of the left EmC/EC. This ventral pathway connects the main language-related brain areas in the superior temporal region and the inferior frontal cortex and may be an alternative connection to the classical dorsal pathway. These results converge with recent literature suggesting that the ventral pathway may have an important role during language learning and processing when the classical dorsal pathway is not available due to insufficient maturation, lesion, or saturation of the WM rehearsal mechanism.

Supplementary Material

Supplementary material can be found at: <http://www.cercor.oxfordjournals.org/>

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Notes

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Supplementary Results and figure captions

LANGUAGE LEARNING UNDER WORKING MEMORY CONSTRAINTS CORRELATES WITH MICROSTRUCTURAL DIFFERENCES IN THE VENTRAL LANGUAGE PATHWAY

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Behavioral experiments

Experiment 2: Irrelevant speech (IS) vs. Baseline (BL)

Although participants from the experiment 1 were able to learn under the IS condition, we carried out a second experiment to assess whether the saturation of the phonological store (IS condition) interfered with learning compared to the baseline (BL) condition without interference.

A new group of fifty-five healthy right-handed participants with similar characteristics to participants from the experiment 1 (mean age, 21.3 ± 2.6 ; 41 women) took part in the experiment 2. These participants were randomly assigned to the segmentation ($n = 28$) or rule learning conditions ($n = 27$). All participants were paid or received course credits.

No significant differences were found between both conditions (IS vs. BL), Language condition (segmentation/rule learning) or their interaction (all $P > 0.1$). Performance in both IS and BL conditions was greater than chance (segmentation condition IS: $t_{27} = 4.6$, $P < 0.0001$, and BL: $t_{27} = 4.6$, $P < 0.0001$; rule learning condition, IS: $t_{26} = 4$, $P < 0.0001$, and BL: $t_{26} = 2.8$, $P < 0.001$) (see Figure S1)). Consistent with the first experiment, these results suggest that interference with the phonological store does not prevent segmentation or rule learning and does not produce interference when compared to a BL condition. Comparing the AS and BL conditions across both experiments (1 and 2) indicated that, in contrast to the IS condition, AS interfered with learning compared to BL. Although performance in the BL and AS conditions was greater than chance (one sample t -test: AS: $t_{51} = 3.2$, $P < 0.01$; BL: $t_{54} = 5.3$, $P < 0.0001$), performance was improved in the BL compared to the AS condition ($t_{105} = -2$, $P < 0.05$, $d = 0.40$). This difference could not be explained by group differences because the IS performance of the two groups did not differ ($t_{105} = -55$, $P > 0.5$, $d = 0.003$).

Experiment 3: Articulatory suppression (AS) vs. Baseline (BL): a between-subjects design

A third behavioral experiment was developed with the aim to evaluate whether the articulatory rehearsal blockade causes a specific impairment in rule learning and speech segmentation when compared to a baseline condition. In addition, the present study used a between-subjects design in order to confirm interference effects of the AS condition, but without any possible confound due to strategic effects that may arise in intra-subject experiments.

Seventy-seven new right-handed participants took part in this experiment (mean age 22.1 ± 4.2 ; 56 women). Participants had similar characteristics to participants in experiments 1 and 2 and they were paid for their participation. Each participant was randomly assigned to one of the four possible conditions (AS condition in a rule learning task: $n = 19$; AS condition in a segmentation task: $n = 19$; BL condition in a rule learning task: $n = 19$; BL condition in a segmentation task: $n = 20$). The materials and procedures were the same as those used in previous experiments except that, in this case, the two working memory conditions compared were an AS condition (as in the first experiment in this article) and a BL condition without constraints. As in experiments 1 and 2, statistical effects were significant when an arcsine transformation was applied to the data.

Univariate ANOVA analysis revealed a main effect of condition (AS/BL) ($F_{1,73} = 8.83$, $P < 0.005$, $\eta_p^2 = 0.11$), supporting the previous effect encountered in the comparisons between Experiments 2 and 1. Thus, although again both conditions were above chance (AS: $54.7 \pm 14\%$, $t_{37} = 2$, $P < 0.05$; BL: $65 \pm 15\%$, $t_{38} = 5.9$, $P < 0.0001$, see Figure S1), performance under the AS condition was impaired as compared to the BL condition ($t_{75} = 3.01$, $P < 0.005$, $d = 0.65$). No differences between segmentation and rule learning were found ($P > 0.1$).

Further DTI-behavioral performance correlations:

Although we found no evidence of a different pattern of WM support to segmentation and rule-learning processes, correlation patterns between individual differences in learning and white matter microstructure were partially task-specific. In the AS condition, the separate analysis of segmentation ($n = 21$) and rule learning ($n = 23$) conditions revealed no significant correlation even at more liberal thresholds ($P < 0.05$, uncorrected). However, the rule learning level under the IS condition correlated with the FA values in the right middle cerebellar peduncle [whole-brain analysis ($P < 0.001$, uncorrected); MNI peak coordinates (X, Y, Z): 31 -48 -33, t -value = 5.07, $P < 0.005$, corrected at cluster level, 60-voxel spatial extent (see Figure S2)]. No significant correlation was found at this threshold for the segmentation group, but again a different pattern of correlations was found at a lower threshold ($P < 0.01$ uncorrected) in the anterior cingulum [MNI peak coordinates (X, Y, Z): -18 30 -5, t -value = 2.54, $P < 0.01$ corrected at cluster level, 60-voxel spatial extent (see Figure S2)]. Although the relevance and function of this path related to our task is still unclear, we highlight this pattern is different from the one obtained in the AS condition.

Figure captions

Figure S1

Distributions of the percentages of correct responses (for segmentation and rule learning together) in the two alternatives forced-choice test for experiment 2 and 3. The test was administered after each language exposure in the irrelevant speech (IS), articulatory suppression (AS) and baseline (BL) conditions. * $P < 0.01$; ** $P < 0.005$. Each point corresponds to an individual participant score, and pentagons denote the group mean for each condition.

Figure S2

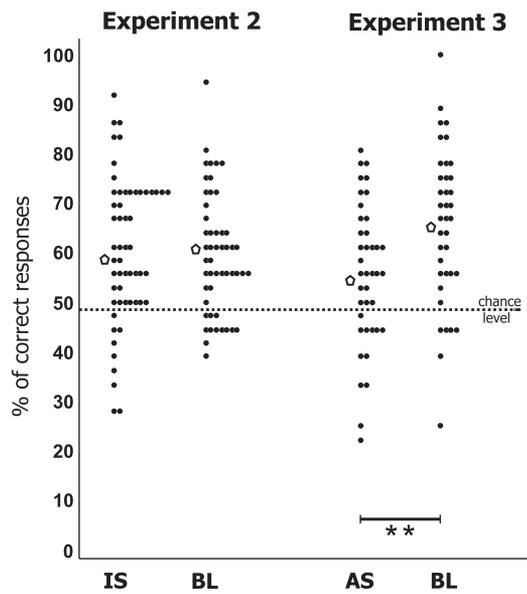
Individual differences in the learning conditions correlated with fractional anisotropy (FA) of major white matter tracts. **A. Left:** for the segmentation condition, significant white matter-correlated clusters rendered on the FA mean image ($P < 0.01$, $n = 60$ voxels). **Right.** Relationship between mean FA value for each participant at the peak of the correlated ROI and performance in the IS condition [left anterior cingulum, peak MNI coordinates $x = -18$, $y = 30$, $z = -5$]. **B. Left:** for rule learning condition, significant white matter-correlated clusters are rendered on the FA mean image ($P < 0.001$, $n = 60$ voxels). **Right:** The relationship between mean FA value for each participant at the peak of the correlated ROI and performance in the IS condition [right middle cerebellar fascicle, peak MNI coordinates $x = 31$, $y = -48$, $z = -33$]. All the results are shown with a more liberal statistical threshold to visualize the white matter pathways ($P < 0.001$; $P < 0.005$; $P < 0.05$; $n = 60$). Color bar indicates the P values.

References

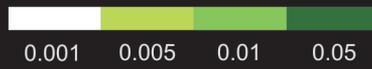
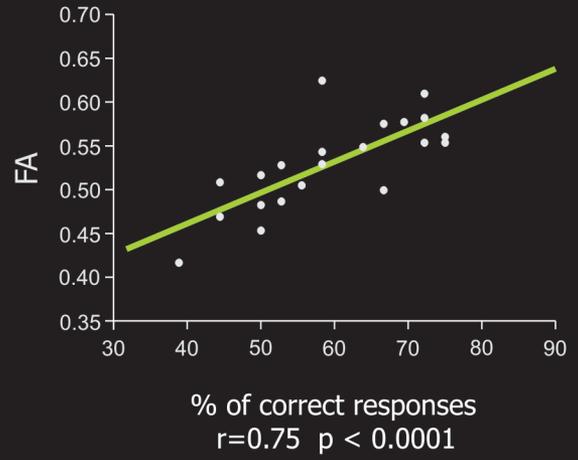
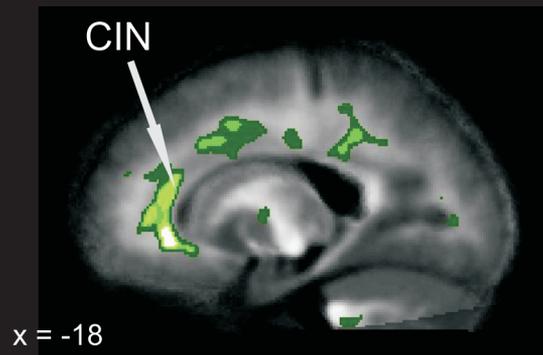
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A



B

