eosinophils are the main secretors of TGF-β1 protein during chronic challenge (*12*). The reason for this disparity is unclear (*4*), but variability in protocols may account for the differences seen in the cell source and expression levels of TGF-β. A number of other factors have been demonstrated to be profibrotic in the lung, notably the chemokine MCP-1, thrombin, endothelin-1, and plasminogen activator inhibitor 1 (*28*). It is difficult to link the presence of these factors to eosinophils specifically. However, the cysteinyl leukotrienes have been shown to be linked to both profibrotic remodeling responses and eosinophils (*29*, *30*). In fact, the eosinophil may be a major source of leukotrienes, often overlooked.

Of importance is that these animal studies are in accordance with observations made in humans. Mild asthmatic patients pretreated with IL-5–specific antibody exhibited significant reduction in tenascin, lumican, and procollagen III (*3*). Our results independently demonstrate that eosinophils are in part responsible for both collagen and smooth muscle changes in a chronic model of asthma. Further, although the contribution of eosinophils to lung dysfunction has been controversial, we show here that eosinophils are not obligatory for airway physiology changes associated with this disease. Taken together, these data provide a rationale for anti-eosinophil–based therapeutics in chronic allergic airways disease.

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References

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Children Creating Core Properties of Language: Evidence from an Emerging Sign Language in Nicaragua

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A new sign language has been created by deaf Nicaraguans over the past 25 years, providing an opportunity to observe the inception of universal hallmarks of language. We found that in their initial creation of the language, children analyzed complex events into basic elements and sequenced these elements into hierarchically structured expressions according to principles not observed in gestures accompanying speech in the surrounding language. Successive cohorts of learners extended this procedure, transforming Nicaraguan signing from its early gestural form into a linguistic system. We propose that this early segmentation and recombination reflect mechanisms with which children learn, and thereby perpetuate, language. Thus, children naturally possess learning abilities capable of giving language its fundamental structure.

Certain properties of language are so central to the way languages operate, and so widely observed, that Hockett termed them "design features" of language (*1*). This study asks whether these properties can arise naturally as a product of language-learning mechanisms, even when they are not available in the surrounding language environment. We focus here on two particular properties of language: discreteness and combinatorial patterning. Every language consists of a finite set of recombinable parts. These basic elements are perceived categorically, not continuously, and are organized in a principled, hierarchical fashion. For example, we have discrete sounds that are combined to form words, that are combined to form phrases, and then sentences, and so on. Even those aspects of the world that are experienced as continuous and holistic are represented with language that is discrete and combinatorial. Together, these properties make it possible to generate an infinite number of expressions with a finite system. It is generally agreed that they are universal hallmarks of language, although their origin is the subject of continued controversy (*2*–*7*).

Humans are capable of representations that lack these properties. For example, nonlinguistic representations such as maps and paintings derive their structure iconically, from their referent. That is, patterns in the representation correspond, part for part, to patterns in the thing represented. In this way, half a city map represents half a city. Unlike language, such nonlinguistic representations are typically analog and holistic.

The present study documents the emergence of discreteness and combinatorial patterning in a new language. Over the past 25 years, a sign language has arisen within a community of deaf Nicaraguans who lacked exposure to a developed language. This situation enables us to discover how fundamental language properties emerge as the nonlinguistic becomes linguistic.

Before the 1970s, deaf Nicaraguan children and adults had little contact with each other. Societal attitudes kept most deaf individuals at home, and the few schools and clinics available

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served small numbers of children. Interviews with former students reveal little evidence of contact with classmates outside school, or after graduation (*8*, *9*). In this context, no sign language emerged, as evidenced by the lack of language in today's adults over the age of 45.

In such situations, deaf people will often develop "home signs": communication systems built up out of common gestures, used with family members. Although not full languages, home signs exhibit some of the rudiments of language (*10*, *11*). The home sign systems developed by Nicaraguans appear to have varied widely from one deaf person to another in form and complexity (*12*).

This situation changed abruptly with the opening of an expanded elementary school for special education in 1977, followed by a vocational school in 1981, both in Managua. Deaf enrollment in the programs initially comprised about 50 students, growing to more than 200 by 1981 and increasing gradually throughout the 1980s. For the first time, students continued their contact outside school hours, and by the mid-1980s deaf adolescents were meeting regularly on the weekends (*8*). Although instruction in school was conducted in Spanish (with minimal success), these first children began to develop a new, gestural system for communicating with each other. The gestures soon expanded to form an early sign language (*13*, *14*). Through continued use, both in and out of school, the growing language has been passed down and relearned naturally every year since, as each new wave of children entered the community (*15*).

Today there are about 800 deaf signers of Nicaraguan Sign Language (NSL), ranging from 4 to 45 years of age. Previous research on NSL has found that changes in its grammar first appear among preadolescent signers, soon spreading to subsequent, younger learners, but not to adults (*16*). This pattern of transmission, when combined with the rapid and recent expansion of NSL, has created an unusual language community in which the most fluent signers are the youngest, most recent learners. Consequently, much of the history of the language can be surveyed by performing a series of observations, progressing from the older signers, who retain much of NSL's early nature, to younger, more recent learners, who produce the language in its expanded, most developed form.

Following this logic, the present study compares the signed expressions of 30 deaf Nicaraguans, grouped into cohorts according to the year that they were first exposed to NSL: 10 from a first cohort (before 1984), 10 from a second cohort (1984 to 1993), and 10 from a third cohort (after 1993). All of the deaf participants have been signing NSL since the age of 6 or younger. Their signed expressions are compared to the gestures produced by 10 hearing Nicaraguan Spanish speakers while speaking Spanish (*17*).

In particular, we examine the gestures and signs in expressions that describe complex motion events, such as rolling down a hill or climbing up a wall. We chose descriptions of motion for two reasons. First, previous research has found that when speakers describe motion events, they often produce co-speech gestures that iconically represent the movement (*18*, *19*). Such gestures (unlike speech) are fully available to deaf observers, likely providing raw materials to shape into a sign language. Second, the description of motion offers a promising domain for detecting the introduction of segmented, linear, and hierarchical organization of information into a communication system. Motion events include a manner of movement (such as rolling) and a path of movement (such as descending). These characteristics of motion are simultaneous aspects of a single event and are experienced holistically. The most direct way to iconically represent such an event would be to represent manner and path simultaneously. Languages, in contrast, typically encode manner and path in separate elements, combined according to the rules of the particular language (*20*). For example, English produces one word to express manner (rolling) and another to express path (down), and assembles them into the sequence "rolling down." Signing that dissects motion events into separate manner and path elements, and assembles them into a sequence, would exhibit the segmentation and linearization typical of developed languages and unlike the experience of motion itself.

To collect samples of signing and gesturing that describe motion events, we presented participants with an animated cartoon and videotaped them telling its story to a peer. Deaf subjects signed their narratives. Hearing subjects spoke Spanish, and only their co-speech gestures were analyzed. Those expressions that included both manner and path information were coded with respect to how the information was integrated: (i) simultaneously, as a single hand movement, and/or (ii) sequentially, articulated separately within a string of simple manner-only and path-only elements (Fig. 1). Note that a single multigesture expression can include both means of integration.

Two analyses compared, across groups, the use of each method of integration. Figure 2A shows the proportion of the expressions produced by each participant that include manner and path simultaneously. All of the Spanish speakers' gestures (1.0) and most of the first-cohort signers' expressions (0.73) use this approach. Second- and third-cohort signers produce relatively fewer expressions of this type (0.32 and 0.38). Figure 2B shows the proportion of expressions produced by each participant that articulate manner and path sequentially. Such sequences are never observed in the Spanish speakers' gestures (0). First-cohort signers sometimes include such sequences (0.27); second- and third-cohort signers include such sequences in most of their expressions (0.78 and 0.73).

In appearance, the signs very much resembled the gestures that accompany speech.

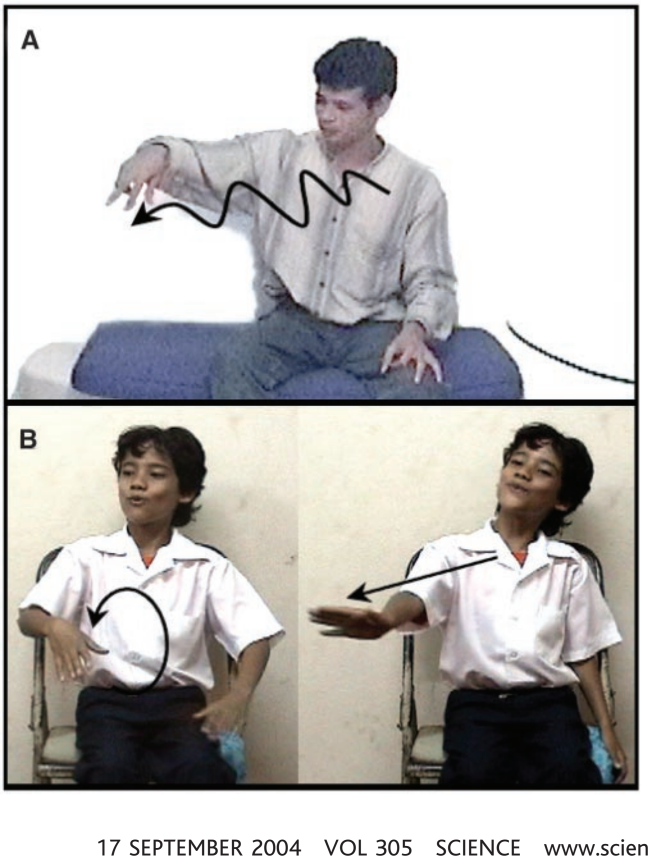

Fig. 1. Examples of motion event expressions from participants' narratives. (**A**) Manner and path expressed simultaneously. This example shows a Spanish speaker describing an event in which a cat, having swallowed a bowling ball, proceeds rapidly down a steep street in a wobbling, rolling manner. The gesture shown here naturally accompanies his speech. Here, manner (wiggling) and path (trajectory to the speaker's right) are expressed together in a single holistic movement. (**B**) Manner and path expressed sequentially. This example shows a third-cohort signer describing the same rolling event in Nicaraguan Sign Language. Here, manner (circling) and path (trajectory to signer's right) are expressed in two separate signs, assembled into a sequence. (The video clips from which the frames were drawn can be viewed at *Science* Online.)

The movements of the hands and body in the sign language are clearly derived from a gestural source. Nonetheless, the analyses reveal a qualitative difference between gesturing and signing. In gesture, manner and path were integrated by expressing them simultaneously and holistically, the way they occur in the motion itself. Despite this analog, holistic nature of the gesturing that surrounded them, the first cohort of children, who started building NSL in the late 1970s, evidently introduced the possibility of dissecting out manner and path and assembling them into a sequence of elemental units. As second and third cohorts learned the language in the mid-1980s and 1990s, they rapidly made this segmented, sequenced construction the preferred means of expressing motion events. NSL thus quickly acquired the discrete, combinatorial nature that is a hallmark of language.

Note that this change to the language, in the short term, entails a loss of information. When representations express manner and path separately, it is no longer iconically clear that the two aspects of movement occurred simultaneously, within a single event. For example, *roll* followed by *downward* might have instead referred to two separate events, meaning "rolling, then descending."

However, the communicative power gained by combining elements more than offsets this potential for ambiguity. Elements and sequencing provide the building blocks for linguistic constructions (such as phrases and sentences) whose structure assigns meaning beyond the simple sum of the individual words. We observed one such structured sequence pattern that has emerged specifically for expressing simultaneity. A sign can be produced before and after another sign or phrase in an A-B-A construction, essentially embedding the second element within the first, yielding expressions such as *roll descend roll*. This string can serve as a structural unit within a larger expression like *cat [roll descend roll]*, or can even be embedded within another sign, as in *waddle [roll descend roll] waddle*, and so on. These A-B-A constructions appeared in about one-third of the coded expressions (0.37) by participants from all three cohorts: four first-cohort signers, seven second-cohort signers, and six third-cohort signers. They were used to link various simultaneous aspects of events, including agent and action (*cat climb cat*), ground and action (*climb pipe climb*), and manner and path (*roll descend roll*). We observed 15 examples of these constructions applied specifically for combining manner and path information, again by signers of all three cohorts: two first-cohort signers, four second-cohort signers, and four third-cohort signers. They never appeared in the gestures of the Spanish speakers, and they represent a temporal hierarchy not found in motion events themselves.

Such hierarchical combinations are central to the language engine, enabling the production of an infinite set of utterances with a finite set of elements. Thus, the emergence of this construction in NSL represents a shift from gesture-like to language-like expression.

It is informative that the first-cohort signers, who originated the language when they were children in the late 1970s, continue to produce it today in a form closer to its gestural model. We take this as an indication of the extent of their impact on NSL before the mid-1980s, when they reached adolescence. The children who were arriving in the mid-1980s then became NSL's second wave of creative learners, picking up where the first cohort left off and making changes that were never fully acquired by now-adolescent first-cohort signers (*15*, *16*). The difference today between first- and second-cohort signers therefore indicates what children could do that adolescents and adults could not. It appears that the processes of dissection, reanalysis, and recombination are among those that become less available beyond adolescence. Such an age effect is consistent with, and would partially explain, the preadolescent sensitive period for language acquisition discussed in other work (*21*, *22*). Using their early learning skills, those who were still children in the mid-1980s developed NSL into the more discrete and combinatorial system that they, and the children who followed in the 1990s, still exhibit today.

Because NSL is such a young language, recently created by children, its changes reveal learning mechanisms available during childhood. Our observations highlight two of these mechanisms. The first is a dissecting, segmental approach to bundles of information; this analytical approach appears to override other patterns of organization in the input, to the point of breaking apart previously unanalyzed wholes. The second is a predisposition for linear sequencing; sequential combinations appear even when it is physically possible to combine elements simultaneously, and despite the availability of a simultaneous model. We propose that such learning processes leave an imprint on languages—observable in mature languages in their core, universal properties—including discrete elements (such as words and morphemes) combined into hierarchically organized constructions (such as phrases and sentences).

Accordingly, these learning mechanisms should influence language emergence and change as long as there are children available to take up a language. Consistent with this account, linear sequencing of elements (even when representing simultaneous aspects of an event) appears to be an initially favored device in language emergence (*23*). For example, strong word order regularities are well documented in creoles, young languages that arise out of particular social situations of language contact (*24*–*26*). Some theories of creolization hold that child learners drive this process (*27*, *28*). Our findings, in line with these approaches, favor a degree of child influence in identifying and sequencing elements (*29*).

However, these learning predispositions will not fully determine a language's eventual structure. For example, many sign languages use simultaneous combinations in addition to sequential ones. Nonetheless, even in cases where adults use simultaneous constructions, the pattern of children's acquisition points to a preference for linear sequencing (*23*). For example, research on the acquisition of American Sign Language (ASL) (*23*, *30*) has shown that children initially break complex

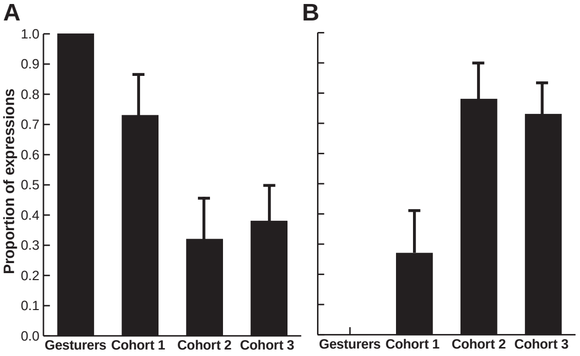

Fig. 2. (**A**) The proportion of expressions that include manner and path that articulate them simultaneously within a single gesture or sign. Proportions were computed for each participant. Bars indicate mean proportions for each of the four groups; error bars indicate SE. All of the co-speech gestures and most of the first-cohort signers' expressions articulated manner and path simultaneously. Second- and third-cohort signers produce relatively fewer expressions of this type. Proportions differ significantly across the four groups (Kruskal-Wallis, $P < 0.02$, $df = 3$, $\chi^2 = 10.8$). Post hoc analyses with Bonferroni adjustment indicate that the Spanish speakers differ significantly from second-cohort signers (Mann-Whitney, $P < 0.04$) and marginally from third-cohort signers (Mann-Whitney, $P < 0.06$). (**B**) The proportion of expressions that include manner and path that articulate them sequentially in a string of manner-only and path-only elements. Proportions were computed for each participant. Bars indicate mean proportions for each of the four groups; error bars indicate SE. These sequential expressions are never observed in the co-speech gestures. First-cohort signers sometimes produce such sequences; second- and third-cohort signers include them in most of their expressions. Proportions differ significantly across the four groups (Kruskal-Wallis, $P < 0.01$, $df = 3$, $\chi^2 = 14.7$). Post hoc analyses with Bonferroni adjustment indicate that the Spanish speakers differ significantly from both second-cohort signers (Mann-Whitney, $P < 0.02$) and third-cohort signers (Mann-Whitney, $P < 0.03$).

verb expressions down into sequential morphemes, rather than produce multiple verb elements together in the single, simultaneous movement found in adult models. In ASL, oversegmentation during acquisition was observed across a number of element types, including the agent and patient of a transitive event, and, as in NSL, the manner and path of a motion event. These elements correspond to semantic units that are relevant to lexicalization patterns in many (possibly all) languages (*20*). Thus, the elements chosen for segmentation may reveal the very primitives that children are predisposed to seek out as basic, grammatical units.

Such primitives, and the processes that isolate and recombine them, are central to children's language-learning machinery today. Whether these drove the formation of the very first human languages depends on whether languages shaped learning abilities, or vice versa. We speculate that a combination of the two was the case. Once language developed a discrete and hierarchical nature, children who tended toward analytical and combinatorial learning would have an advantage acquiring it (*3*). In this way, evolutionary pressures would shape children's language-learning (and now, language-building) mechanisms to be analytical and combinatorial. On the other hand, once humans were equipped with analytical, combinatorial learning mechanisms, any subsequently learned languages would be shaped into discrete and hierarchically organized systems (*4*, *5*).

Although our findings are consistent with both directions of effect in the evolution of learners and languages, they are at odds with accounts in which such attributes evolved externally, were passed from generation to generation solely through cultural transmission, and were never reflected in the nature of the learning mechanism (*7*). In studies of mature languages, the potential imprint of the learning mechanism is redundant with, and hence experimentally obscured by, preexisting language structure. But the rapid restructuring of Nicaraguan Sign Language as it is passed down through successive cohorts of learners shows that even where discreteness and hierarchical combination are absent from the language environment, human learning abilities are capable of creating them anew.

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Movies S1 and S2

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Two Distinct Actin Networks Drive the Protrusion of Migrating Cells

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Cell migration initiates by extension of the actin cytoskeleton at the leading edge. Computational analysis of fluorescent speckle microscopy movies of migrating epithelial cells revealed this process is mediated by two spatially colocalized but kinematically, kinetically, molecularly, and functionally distinct actin networks. A lamellipodium network assembled at the leading edge but completely disassembled within 1 to 3 micrometers. It was weakly coupled to the rest of the cytoskeleton and promoted the random protrusion and retraction of the leading edge. Productive cell advance was a function of the second colocalized network, the lamella, where actomyosin contraction was integrated with substrate adhesion.

Cell migration involves a coordinated cycle of plasma membrane protrusion at the leading edge, adhesion site formation under the protrusion, disruption of older adhesion sites at the cell rear, and cytoskeleton contraction against adhesions to yield cell body movement (*1*). Protrusion is thought to result from actin filament (F-actin) polymerization against the plasma membrane (*2*), with the polymerization rate regulated by the rate of monomer addition to the fast-growing ("barbed") ends of filaments. This may depend on actin-related protein 2/3 (Arp2/3) complex activation, which creates free barbed ends by branching and de novo nucleation of filaments (dendritic nucleation) (*3*), and on actin depolymerizing factor (ADF) cofilin, which creates free barbed ends by severing preexisting filaments and promoting depolymerization of free filament "pointed" ends (*4*). Filament growth is limited by barbed end–capping