linear function of the cosine of the emission angle. 12. This work was based on observations made with the NASA/European Space Agency HST, obtained at the Space Telescope Science Institute (STScI), which is operated by the Association of Universities for Research in Astronomy under NASA contract NAS5-26555. Support was provided by NASA through grant number GO-07429.01–97A from STScI. I thank M. Tomasko for his support and the crew at STScI for their cooperation with special requests for scheduling and implementation. The NICMOS camera team made these observations possible.

Brain Activity During Speaking: From Syntax to Phonology in 40 Milliseconds
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In normal conversation, speakers translate thoughts into words at high speed. To enable this speed, the retrieval of distinct types of linguistic knowledge has to be orchestrated with millisecond precision. The nature of this orchestration is still largely unknown. This report presents dynamic measures of the real-time activation of two basic types of linguistic knowledge, syntax and phonology. Electrophysiological data demonstrate that during noun-phrase production speakers retrieve the syntactic gender of a noun before its abstract phonological properties. This two-step process operates at high speed: the data show that phonological information is already available 40 milliseconds after syntactic properties have been retrieved.

From early in life we acquire knowledge about the words in our language. This knowledge includes information about the meaning of words, their syntactic properties (such as word class), and their phonological properties (such as their phonemes and syllable structure). All this information is stored in a component of long-term memory that is usually referred to as the mental lexicon. During speaking, the mental lexicon is accessed automatically at very high speed to select words that express the intended meaning, and to retrieve their syntactic and phonological properties. These properties are used to structure the words according to the syntactic constraints of one’s language and to build up the sound pattern of an utterance. A central unresolved question concerns the orchestration in real time of the retrieval of the distinct types of linguistic knowledge required to produce fluent speech (1, 2). The activation of this knowledge necessarily precedes articulation, but only by a fraction of a second, given the speed with which we speak. Data from behavioral studies as well as from neuropsychological studies of patients with language impairment have suggested that a word’s semantic and syntactic properties are retrieved before its phonological form is constructed (2, 3). We have now obtained direct evidence on the real-time activation of syntax and phonology in Dutch noun-phrase production. We found that the syntactic gender of a noun is retrieved about 40 ms earlier than its first phonological segment.

The main experimental task was the production of noun phrases in Dutch. Participants (4) were presented with colored pictures of objects and animals, which they were instructed to name using a noun phrase without a definite article (such as “rode tafel,” red table). On half of the trials they performed a syntactic-phonological classification task before producing the noun phrase. The classification task consisted of the conjunction of a go/no-go decision and a left- or right-hand response. In the first experiment, the response hand was determined by the syntactic classification, and the phonological classification determined whether or not a push-button response should be given (Fig. 1) (3). The syntactic and phonological properties of the word that are required to perform the classification tasks become available automatically through the speech production system. The syntactic classification involved determining the gender of the noun. In Dutch, as in, for example, French and German, nouns are characterized by syntactic gender. This is a purely syntactic property that needs to be retrieved from the mental lexicon during noun-phrase production to determine the definite article of the noun (“de” for common gender, and “het” for neuter gender), or the adjectival suffix when no definite article is used in the noun phrase (“-e” for common gender, and no suffix for neuter gender). The phonological classification involved determining the word-initial pho-
that is directly related to the preparation for (LRP) (Fig. 2). The LRP is a brain potential derived the lateralized readiness potential was time the left and right motor cortices. From the potentials from electrode sites located above the left and right motor cortices. These difference waveforms are averaged separately for trials in which the left versus the right hand is cued. (B) Second, to cancel out lateralized potentials that are not specifically related to response preparation, we subtracted the waveform obtained for the left-hand trials from the waveform obtained for the right-hand trials. The resulting LRP reflects the average amount of lateralization occurring as a result of the motor preparation of the response hands. The LRP deviates from the base line in an upward direction as soon as response preparation for the cued response hand occurs (7, 8).

To measure the moments at which syntactic and phonological information became available to execute the classification task, we recorded event-related brain potentials from electrode sites located above the left and right motor cortices. From the averaged electrophysiological activity that was time-locked to picture onset, we derived the lateralized readiness potential (LRP) (Fig. 2). The LRP is a brain potential that is directly related to the preparation for motor actions (6–8). It has been shown to develop as soon as task-relevant perceptual and cognitive information is available for the motor system and to be sensitive to low levels of response activation that do not result in an overt response (8–10). As such, the LRP can be used to detect the moments at which syntactic gender and word-initial phoneme information become available for response preparation. The logic behind the procedure is that if during noun-phrase production syntactic retrieval precedes the retrieval of phonological form, the results of the syntactic gender classification will be transmitted to the response system earlier than the results of the word-initial phoneme classification. In this case, preparation of the response hand can start on the basis of syntactic information before phonological information informs the individual whether to respond. This is precisely what we observed. An LRP developed not only for go trials, but initially also for no-go trials, without an overt response (Fig. 3) (11). The early availability of syntactic information enabled response preparation, but when information about the noun’s phonological form became available, this then overruled further response preparation on the no-go trials.

A possible concern might be that both types of information become available at the same moment in time during noun-phrase production, but that because of the task configuration, the response hand is always selected before the go or no-go decision is made. Therefore, we performed a second experiment in which the same task components were used, but now it was the syntactic gender information that determined the go or no-go decision and the word-initial phoneme that determined the response hand. This task configuration emphasizes the early use of phonological information: Previous LRP studies have shown that in a choice reaction go or no-go task, participants assign priority to the extraction of stimulus information that can be used to select a response hand (9), which in experiment 2 is the phonological information. Nevertheless, if syntax is indeed available before phonology, then an LRP should develop only on go trials and not on no-go trials. This is exactly the pattern of results that we observed (Fig. 4). The presence of a no-go LRP in experiment 1 together with its absence in exper-
iment 2 demonstrates that in noun-phrase production the syntactic gender of a noun is retrieved before its abstract phonological properties. By comparing the go LRP with the no-go LRP obtained in experiment 1, we can estimate the length of the time interval in which syntactic but no phonological information of the noun was available. Two time points are of interest from this comparison (Fig. 3). First, the go and no-go LRPs started to develop at about 370 ms after picture onset, so at that moment, syntactic gender was available to select the correct response hand. Second, at about 410 ms after picture onset the go and no-go LRPs diverged sharply. While the go LRP continued to develop, the no-go LRP gradually returned to the base line. This indicates that there was already enough phonological information available at 40 ms after LRP onset to make the go or no-go distinction. Thus, in noun-phrase production it takes only about 40 ms to retrieve a noun’s initial phoneme once its syntactic gender has been retrieved. These data provide fine-grained temporal information about the moments at which distinct word representations are retrieved from the mental lexicon during the real-time process of speaking. The empirical approach that we have presented opens the way for further, temporally fine-grained neurophysiological analyses of the uniquely human skill of speaking.

REFERENCES AND NOTES

4. Thirty-two right-handed students between 21 and 29 years of age took part in the experiments. All were native speakers of Dutch and had normal or corrected-to-normal vision, and none had any neurological impairment or had experienced any neurological trauma according to their answers to a questionnaire.
5. The materials consisted of 48 colored line drawings depicting objects and animals with morphologically simple names. Half of the picture names had common gender, and the other half had neuter gender. These words were matched for word frequency, number of syllables, and word length. There were no clear semantic differences between the sets of common and neuter gender words. Two sets of pictures were constructed. In one set the names of the pictures started with the phonemes /b/ and /s/, and in the other set the names of the pictures started with the phonemes /k/ and /b/. Each of the phonemes was represented equally often in the picture sets. To control for material-specific effects, we rotated the assignment of the four response types to the different picture categories across participants in such a way that each picture contributed equally to each of the response types. Each target picture was presented to each participant four times in naming-only trials and six times in trials that required the additional classification task. A fixed hand response was required at the presentation of a fixation cross. After 1500 ms a picture was presented for 2500 ms in either the color yellow or red. Participants were instructed to name the colored picture as quickly as possible using a noun phrase without a determiner. On half of the trials a frame appeared around the picture at 150 ms after picture onset, signaling that the classification task had to be carried out and naming had to be delayed. The syntactic classification involved a decision about the noun’s definiteness (def/def* or *hes*), and the phonological classification involved a decision about the word’s initial phoneme (for example, /b/ or /s/). For go trials, participants made a hand response by pressing with their index finger either the button on the left side or the button on the right side of the chair in which they were seated. For no-go trials participants did not press any of the buttons. At 1650 ms after picture onset the frame disappeared, and participants had to produce the appropriate no-determiner noun phrase.
11. Trials on which participants produced utterances other than the appropriate ones or gave an incorrect hand response were eliminated from the data. Incorrect hand responses were defined as go trials in which electromyogram (EMG) activity was detected on the incorrect response side, and no-go trials in which EMG activity occurred. In experiment 1 error rates were 4.8 and 1.5% for go and no-go trials, respectively. In experiment 2 error rates were 4.9 and 3.1% for the go and no-go trials, respectively. All single-trial waveforms containing incorrect artifacts in the time window of 200 ms before picture onset to 1500 ms after picture onset were removed from the data. Per participant, the minimum number of trials left for averaging was 35 per condition. For each single-trial waveform the average voltage in the 200-ms period preceding picture onset was subtracted from the voltage at all following time points. LRPs were derived separately for the go and no-go conditions. To test for the presence of an LRP and to estimate its onset, we performed analyses on 50-ms intervals, starting from frame onset in sequential steps of 10 ms (for example, 150 to 200 ms, 160 to 210 ms, and so on). For each window a one-tailed t test with a 95% confidence interval was performed to test whether the mean voltage within the window exceeded the mean voltage within the base-line interval. An LRP was defined to be present if five or more consecutive windows resulted in a significant t value. The onset of the first of these windows was taken to be the LRP onset latency. To determine the point of divergence between the go and no-go LRPs, we subtracted the average voltage at each individual time point of the no-go waveform from the average voltage at the corresponding time points of the go waveform. We performed one-tailed t tests to test whether the mean go and no-go difference scores differed significantly from zero, using the same procedure as described for the individual LRP waveforms.
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Targeting the Receptor-Gα Interface to Inhibit in Vivo Pressure Overload Myocardial Hypertrophy

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Hormones and neurotransmitters may mediate common responses through receptors that couple to the same class of heterotrimeric guanine nucleotide–binding (G) protein. For example, several receptors that couple to Gβγ class proteins can induce cardiomyocyte hypertrophy. Class-specific inhibition of Gq-mediated signaling was produced in the hearts of transgenic mice by targeted expression of a carboxyl-terminal peptide of the α subunit Gqα. When pressure overload was surgically induced, the transgenic mice developed significantly less ventricular hypertrophy than control animals. The data demonstrate the role of myocardial Gqα in the initiation of myocardial hypertrophy and indicate a possible strategy for preventing pathophysiological signaling by simultaneously blocking multiple receptors coupled to Gqα.

Myocardial hypertrophy is an adaptive response to various mechanical and hormonal stimuli and represents an initial step in the pathogenesis of many cardiac diseases that ultimately progress to ventricular failure. The mechanisms by which cardiac hypertrophy is initiated and how this condition eventually progresses to heart failure are poorly understood. Several independent signaling pathways have been implicated in the activation of the hypertrophic response in vitro (1). The G protein Gqα is thought to be important in this process because various ligands, such as phenylephrine, angiotensin II (AngII), and endothelin I, that activate Gqα-coupled receptors can trigger hypertrophic responses in cultured myocytes (2). In vivo studies with Gqα-coupled receptor antagonists have also implicated Gqα-mediated signaling in pressure-overload ventricular hypertrophy (3), and transgenic mice with cardiac overexpression of either Gqα, αqα,