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The influence of syllable onset complexity and syllable frequency on speech motor control

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Abstract

Functional imaging studies have delineated a "minimal network for overt speech production", encompassing mesiofrontal structures (supplementary motor area, anterior cingulate gyrus), bilateral pre- and postcentral convolutions, extending rostrally into posterior parts of the inferior frontal gyrus (IFG) of the language-dominant hemisphere, left anterior insula as well as bilateral components of the basal ganglia, the cerebellum, and the thalamus. In order to further elucidate the specific contribution of these cerebral regions to speech motor *planning*, subjects were asked to read aloud visually presented bisyllabic pseudowords during functional magnetic resonance imaging (fMRI). The test stimuli systematically varied in onset complexity (CCV versus CV) and frequency of occurrence (high-frequency, HF versus low-frequency, LF) of the initial syllable. A cognitive subtraction approach revealed a significant main effect of syllable onset complexity (CCV versus CV) at the level of left posterior IFG, left anterior insula, and both cerebellar hemispheres. Conceivably, these areas closely cooperate in the sequencing of subsyllabic aspects of the sound structure of verbal utterances. A significant main effect of syllable frequency (LF versus HF), by contrast, did not emerge. However, calculation of the time series of hemodynamic activation within the various cerebral structures engaged in speech motor control revealed this factor to enhance functional connectivity between Broca's area and ipsilateral anterior insula.

Keywords: Functional magnetic resonance imaging; Bisyllabic pseudowords; Complexity; Frequency; Functional connectivity

1. Introduction

As a rule, recent models of spoken language production make a distinction between higher-order ("planning") and lower-level ("execution") aspects of speech motor control. For example, Levelt and coworkers (1999) postulated a computational stage, i.e., "phonetic encoding", which transforms more abstract ("phonological") word forms into motor programs, whereas a subsequent "articulator" translates these routines into the neural signals, "steering" the movements of the vocal tract. A similar hierarchy of control systems, usually, is assumed in the clinical literature, allowing for a separation of disorders of speech motor planning, i.e., apraxia of speech (AOS), and dysfunctions of speech motor execution, i.e., the dysarthrias (e.g., Duffy, 2005).

As a salient neuroanatomical characteristic, AOS represents a syndrome of the language-dominant hemisphere, almost exclusively bound to left-sided infarctions within the area of blood supply of the middle cerebral artery (Ackermann & Ziegler, in press). By contrast, unilateral supratentorial lesions rarely—if at all—give rise to severe and persisting dysarthria. Hence, unlike more basic motor

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execution processes, which are assumed to be organized in a bilateral fashion, the higher-order planning aspects of speech motor control show the same cerebral lateralization effects as the "core psycholinguistic language functions" (e.g., Caplan, 1987). The intra-hemispheric lesion site of AOS, however, is still a matter of dispute (for a review, see Ziegler, 2008). Based upon clinico-neuroanatomical correlation studies, the major hypotheses either focus upon posterior parts of the left inferior frontal gyrus (IFG; Broca, 1861; Hillis et al., 2004), ipsilateral anterior insular cortex (Dronkers, 1996), or the "face/mouth area" of the motor strip of the language-dominant hemisphere, including adjacent white matter structures as well as the anterior limb of the internal capsule (Fox, Kasner, Chatterjee, & Chalela, 2001; Schiff, Alexander, Naeser, & Galaburda, 1983; Tanji et al., 2001).

Increasingly, functional imaging techniques now are applied within the domain of the speech sciences (Ackermann, Riecker, & Wildgruber, 2004b). The first systematic account of the cerebral circuitry bound to motor aspects of language production emerged as the by-product of a positron emission tomography (PET) investigation of lexical aspects of single-word processing (Petersen, Fox, Posner, Mintun, & Raichle, 1989). Subtraction of the hemodynamic responses to passive auditory/visual application of common nouns from the BOLD effects associated with overt repetition of such items was assumed to isolate the cerebral structures related to motor aspects of speech production. Besides supplementary motor area (SMA), sensorimotor cortex, and anterior–superior components of the cerebellum, an activation spot "buried" in the depth of the lateral sulcus could be detected. By contrast, Broca's area did not show any significant reactions. In line with several previous sporadic observations (see Ackermann et al., 2004b, for a review), a subsequent PET study confirmed these findings of left-hemisphere intrasylvian hemodynamic activity related to motor aspects of speech production and, more specifically, was able to assign this response to the anterior insula (Wise, Greene, Büchel, & Scott, 1999). Rostral intrasylvian cortex was assumed to represent the neural substrate of the planning stage of speech motor control, since a preceding clinico-neuroradiological correlation study had found cerebral lesions in AOS patients to be centered around the anterior insula (Dronkers, 1996).

As an alternative approach, a recent study of our group used the technique of functional connectivity analysis to further delineate the cerebral correlates of higher-order and lower-level aspects of speech motor control (Riecker et al., 2005). The exploration of the temporal dynamics of the cerebral hemodynamic activation patterns during syllable repetitions revealed the cortical and subcortical brain regions engaged in this task to be organized into two networks: high correlations emerged between (i) left SMA, left anterior insula, left dorsolateral frontal cortex, including Broca's area, and superior parts of the cerebellum, on the one hand, and (ii) sensorimotor cortex, thalamus, putamen/pallidum, left caudatum and inferior cerebellum, on the other. In consideration of the differential time course of the BOLD responses within these regions, the two networks were—tentatively—assigned to (i) the preparation/initiation and (ii) the execution of speech movements, respectively.

A straightforward functional imaging approach towards a separation of planning and executive components of the brain network of speech motor control should—most obviously—be based, first, on a computational description of the processing stages involved and, second, on experimental paradigms, derived from these theoretical suggestions. The most elaborated contemporary model of language production, put forward by Levelt and coworkers (1999), assumes phonetic planning to be centered around the retrieval and assembly of syllable-sized motor programs. Within this conceptual framework, the computational load of higher-order aspects of speech motor control must be expected to vary, in the first instance, with *syllable frequency*: Whereas the encoding of high-frequency (HF) syllables simply requires access to a "mental syllabary", i.e., a store of highly automatized, pre-compiled, holistic motor routines representing entire syllable structures, items of a low frequency (LF) of occurrence must be assembled from smaller bits, e.g., from phonemes. As a consequence, the sub-syllabic route requires enhanced effort and, thus, poses higher temporal demands upon phonetic planning (Cholin, Levelt, & Schiller, 2006). In line with these suggestions, AOS subjects produce more errors in association with LF as compared to HF syllables (Aichert & Ziegler, 2004; Staiger & Ziegler, in press).

On the basis of Levelt's theory of language production, experimental variation of syllable frequency should represent the most adequate probe of phonetic encoding operations. However, apart from a small number of studies of visual word processing (Carreiras, Mechelli, & Price, 2006), the available functional imaging studies of speech motor control have not strictly controlled for this factor. A recent fMRI investigation by Shuster and Lemieux (2005), for instance, assumed the computational load of phonetic encoding mechanisms to increase in parallel with word length. They found the contrast between four- and monosyllabic nouns not to be associated with any significant hemodynamic effects at the level of the left anterior insula and concluded that motor planning processes during language production do not engage intrasylvian cortex. However, the test materials used in this study were controlled for *word* but not for *syllable* frequency. It cannot be ruled out, therefore, that the monosyllabic items predominantly consisted of LF syllables while their longer cognates were composed of HF units. As a consequence, the expected impact of word length upon phonetic encoding processes might have been masked, and the observed distributional pattern of hemodynamic responses reflect unspecific effects of the longer test materials, e.g., increased articulatory effort.

Another recent model-driven study varied the two factors *within-syllable complexity* (simple versus complex syllable onset) and *between-syllable complexity* (re-iteration

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of the same token versus switching between three different items) in an orthogonal fashion to further elucidate the brain network bound to the preparation and the overt production of trisyllabic nonwords (Bohland & Guenther, 2006). An increase in sequential complexity of the test materials gave rise, among others, to enhanced hemodynamic activation of the left inferior frontal sulcus and left posterior parietal areas as well as bilateral responses of anterior insular and ventral motor/premotor areas, concomitant with a strong lateralization effect towards the language-dominant hemisphere. By contrast, sub-syllabic complexity, the second factor considered, yielded predominantly bilateral main effects, especially at the level of mesiofrontal and rostral intrasylvian cortex, the frontal operculum, and the cerebellum. However, this study also failed to systematically control for syllable frequency. As concerns the dimension *within-syllable complexity*, items with an initial consonant cluster are often less frequent than simple CV units. Variation of this factor, thus, might be confounded by syllable frequency. The concept of a mental syllabary, furthermore, assumes that onset complexity does not matter at the level of pre-compiled, holistic motor routines. Within the framework of that model, thus, complexity of syllable onset per se does not affect phonetic encoding processes. The theoretical status of the second dimension of the two-factorial experimental design considered by Bohland and Guenther (2006), i.e., *complexity of syllable sequence*, also raises questions. Levelt's model of speech production does not account for an impact of this dimension upon phonetic encoding, since the process of compiling two or more successive syllables is assigned to the stage of motor *implementation* rather than motor programming (Levelt, Roelofs, & Meyer, 1999). Indeed, there is some evidence that the concatenation of two different syllables specifically challenges AOS patients (Deger & Ziegler, 2002), but a specific role of this operation in phonetic encoding has not been proved for normal speakers. Furthermore, repeated access to the same syllable three times in a row need not necessarily be less demanding than the encoding of three different successive syllables, since activation of the same unit might be hampered by refractory processes. In conclusion, the available functional imaging studies do not allow for a distinct separation of planning from execution processes within the domain of speech motor control and, hence, do not provide an unambiguous model-based account of the cerebral correlates of phonetic encoding in speech production.

In order to accomplish a more precise differentiation of the stage of phonetic planning from motor execution processes, as conceptualized in current psycholinguistic models, the test materials of the present fMRI study of overt speech production were systematically controlled for syllable frequency. As a second factor, complexity of syllable onset was varied in an orthogonal fashion to the former dimension. Onset complexity must be expected to have—within the framework of Levelt's model—an impact upon phonetic encoding, since LF syllables have to be assembled from smaller constituents (Levelt et al., 1999). Hence, this psycholinguistic theory would predict that the neural network engaged in speech motor planning is sensitive to changes in syllable frequency and, within the domain of LF items, to changes in onset structure. A role of subsyllabic complexity, over and above the influence of syllable frequency, can also be expected on the basis of clinical data demonstrating that patients with phonetic encoding impairments are sensitive to the complexity of syllable constituents (e.g., Staiger & Ziegler, in press).

As a test of these predictions, bisyllabic nonwords, consistent with the phonotactic rules of German, were visually presented during fMRI measurements, and subjects were asked to read them as fast as possible. The test items were characterized by a trochaic pattern, i.e., the unmarked accent pattern of German, with the target units in the first (stressed) and a constant syllable in the second (unstressed) position. Besides a cognitive subtraction approach, functional connectivity analysis was applied to the obtained data set (Riecker et al., 2005), in order to identify brain structures characterized by a similar time course of hemodynamic activation.

2. Methods

2.1. Subjects

The present study recruited nine subjects (native speakers of German; age: 20–37 years, mean age = 28.4 years; 5 women), none of them reported a history of neurologic, psychiatric, or medical diseases. At clinical examination, hearing and visual capacities were found uncompromised. Informed consent had been obtained in line with the Declaration of Helsinki and the Institutional Review Board of the University of Ulm. All participants were right-handed according to the Edinburgh handedness scale (inclusion criterion = lateralization index > 80%).

2.2. Test materials

Altogether, 64 bisyllabic pseudowords, consistent with the phonotactic rules of the German language, served as test materials (four stimulus types × 16 different tokens per stimulus type, see below). To avoid confounding interactions between syllable frequency and segmental onset complexity of the two successive syllables, all items encompassed the same (unstressed) second unit, i.e., /tet/. This approach was based upon semantic ratings of the test materials, conducted by ten undergraduate students at the Institute for Natural Language Processing, University Stuttgart: Pseudowords with /tet/ as the second syllable turned out to show the least density of associations as compared to items containing other final syllables. The initial syllable of the nonsense words was systematically varied both in segmental onset complexity and frequency of occurrence (CV.tet versus CCV.tet, HF versus LF items; two-factorial experimental design), giving rise to four stimulus categories: simple-HF,

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complex-HF, simple-LF, and complex-LF. For each stimulus group 16 different items were generated (see Appendix). Since two stimuli out of each set were repeated three times during the fMRI measurements, each run of the experiment included altogether 20 pseudowords of the same category (total of 4 × 20 items).

The control for frequency of occurrence in standard German included two steps of item selection.

(i) A set of computational phonotactic techniques, developed at the Institute for Natural Language Processing, University of Stuttgart, allows for the calculation of syllable frequency distributions, based upon a multivariate clustering approach (Müller, 2002; Müller, Möbius, & Prescher, 2000). This algorithm, trained on a large, balanced corpus of German words (31 million lexical items), takes five dimensions of a syllable into account: segmental structure of onset, nucleus, and coda each, intra-word position, and stress status. The obtained frequency counts are more valid than estimates derived solely from the segmental make-up of syllables.

(ii) The frequency ranks of the selected items were compared to the frequency values of sublexical units of the "Munich Syllable Frequency List" (Aichert, Marquardt, & Ziegler, German Database for Sublexical Frequencies and Structures, EKN, Munich, unpublished). This list is based on the CELEX-corpus (365,530 word forms; Baayen, Piepenbrock, & van Rijn, 1995).

Both the Stuttgart (Müller, 2002) and the Munich lists have been derived from corpora based on spoken and written words.

Using these two instruments, the mean rank of each selected syllable could be determined. The HF items were characterized by a rank between 1 and 500 (mean = 271), their LF cognates by a rank exceeding 1200 (mean = 2449).

2.3. Procedure

The entire experiment encompassed two runs. During each session, 80 bisyllabic pseudowords were presented block-wise via head-mounted video-glasses. Each run encompassed 4 blocks of each of the four stimulus categories, resulting in 16 blocks, presented in a pseudo-randomized and counterbalanced order. Within a block five different items of the same category were displayed for 1.5 s each, preceded by a fixation cross. The inter-stimulus-intervals within a block amounted to 2.5 s (total block duration = 17.5 s). Each run started with a baseline interval (continuous presentation of a fixation cross, duration = 9 s) which also separated subsequent blocks (total length of a run = 433 s; inclusive dummy scans 7.5 min).

Subjects had been instructed to read the stimuli aloud as soon as possible after visual presentation (see Fig. 1 for a schematic representation). Responses were recorded on a computer in digitized form, using a microphone insensitive to the magnetic environment and positioned close to the subjects' mouth inside the head coil.

2.4. fMRI scanning

Subjects lay supine in a 3.0 T head scanner (Siemens Allegra; Siemens, Erlangen, Germany), their heads being secured by foam rubber in order to minimize movement artefacts. Using an echo-planar imaging sequence (64 × 64 matrix, field of view = 192 × 192 mm^2, TE = 35 ms, TR =

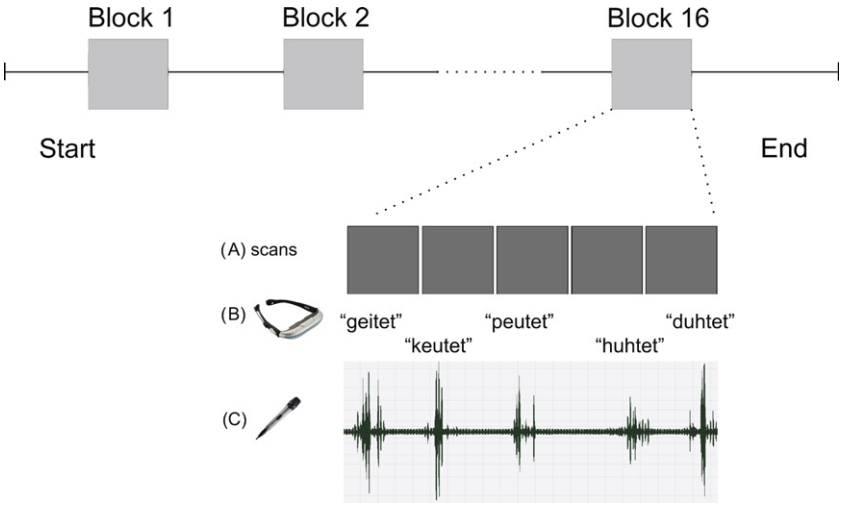

Fig. 1. Schematic representation of the experimental set-up (5 out of 160 nonsense syllables consisting of four categories with an increasing degree of difficulty: simple and high-frequency syllables, simple and low-frequency syllables, complex and high-frequency syllables, and complex and low-frequency syllables). (A) Time course of scan acquisition: Each box represents the measurements across one complete brain volume comprising 36 slices (repetition time (TR = 3 s)). (B) After a baseline of about 15 s the respective nonsense syllables were presented via video-glasses in a pseudo-randomized and counterbalanced order. (C) Subjects were instructed to read the visually displayed syllables aloud and their speech productions were recorded.

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3 s, flip angle = 90 °), 36 parallel axial slices (thickness = 3 mm, gap = 0.75 mm) were obtained across the entire brain volume (2 runs × 155 images, resulting, altogether, in 310 image volumes), including five initial dummy scans (equilibration of T1 saturation effects). For the sake of anatomical localization of hemodynamic activation effects, fMRI maps were superimposed on a T1-weighted 3D sequence, averaged across all subjects (MPRAGE; 208 sagittal slices, thickness = 1.0 mm, 256 × 256 matrix, field of view = 256 × 256 mm^2, TE = 4.38 ms, TR = 5.5 ms).

Head displacements during fMRI measurements interact with spin excitation history and, thus, may modify the BOLD signals of the respective scans. Based upon a series of previous studies, it was decided to exclude *a priori* all data sets from further signal analysis with a range of motion exceeding a threshold of 2 mm in any direction. Furthermore, the head movement parameters were checked in all (*x*-, *y*- and *z*-) dimensions after the realignment step of signal preprocessing. No subject had to be excluded, probably, because the participants had performed several test runs outside and inside the scanner prior to fMRI measurements in order to get familiar with the experimental setting and to learn how to avoid more pronounced movements.

2.5. Signal analysis

2.5.1. Data preprocessing

Analysis of the fMRI data was based upon the SPM5 software package (Wellcome Institute of Cognitive Neuroscience, London, UK). After realignment of each anatomical T1-weighted image to the standard T1 template provided by SPM5, the functional data sets were co-registered, based upon the same transformation matrix. Subsequently, spatial normalization and correction of MRI images into a standard space as defined by an ideal template was performed. Finally, the normalized data sets were smoothed by means of an isotropic Gaussian kernel (full-width at half maximum = 10 mm).

2.5.2. Cognitive subtraction analysis and hemodynamic main effects

In order to determine the influence of syllable onset structure and syllable frequency on the magnitude of BOLD signal changes, several pair-wise cognitive subtractions of the hemodynamic responses (One-way ANOVA) were performed: CCV versus CV, LF versus HF, CCV/LF versus CV/HF, CV/LF versus CCV/HF, and vice versa. In addition, the hemodynamic main effects across all syllable categories and subjects were calculated, providing the basis for the selection of volumes of interest (VOI), required for functional connectivity analysis (see below). For anatomical localization of activation "spots", the fMRI maps were superimposed on transverse sections of the structural MR images averaged across all subjects. The height threshold of the present study at the voxel level was set at $p < .001$ ($T > 3.10$), using an extent threshold of $k \geqslant 46$ voxels. The extent threshold "*k*" defines the minimum size of activation clusters entered into statistical analysis ($n \times$ voxels).

2.5.3. Analysis of fMRI time series ("functional connectivity")

The notion of brain connectivity represents an elusive concept, varying across different areas of research (Horwitz, 2003). As concerns functional imaging, functional connectivity has been defined, based upon a consensus workshop (Lee, Harrison, & Mechelli, 2003), as the "temporal correlation between spatially remote neurophysiological events" (Friston, Frith, & Frackowiak, 1993). To obtain a measure of functional connectivity of hemodynamic activation, region-specific time series of BOLD signal changes were compared to each other. Individual "subtraction data" (see above) provided the vantage point for this approach. The region-specific time series within each VOI included the first eigenvariate of all voxels within a 5 mm radius sphere, centered around the respective local maximum. Afterwards, all VOIs of a subject were compared with each other. Thus, the within-subject correlation matrices across all region-specific time series could be calculated. Subsequently, group means and standard deviations were determined across all subjects. Using SPSS for windows (Norusis, 1994), the computed coefficient values then could be assigned to one of the categories "very high", "high", and "intermediate correlation", respectively (for further details, see Riecker et al., 2005).

3. Results

3.1. Behavioral data

The produced pseudowords of each subject were recorded during the fMRI experiment. After completion of the measurements, subjects did not report to have experienced any extra effort in association with the reading task. Furthermore, the performed analysis demonstrated an error rate of pseudoword reading of 2.83 ± 0.45% (mean/standard deviation).

3.2. fMRI data

3.2.1. Hemodynamic main effects

In order to select the VOI required for functional connectivity analysis, the hemodynamic main effects across all syllable categories and subjects were calculated. Fig. 2 displays the areas of significant activation, and Table 1 provides the respective quantitative data. The respective cerebral network encompasses (i) mesiofrontal regions, extending from SMA proper in anterior–ventral direction to pre-SMA and the anterior cingulate cortex, (ii) ventral parts of the pre- and postcentral convolutions, (iii) IFG of the left hemisphere, (iv) intrasylvian areas, (v) the superior temporal lobe, encroaching upon inferior parietal cortex, (vi) the thalamus, (vii) putamen/ pallidum, and (viii)

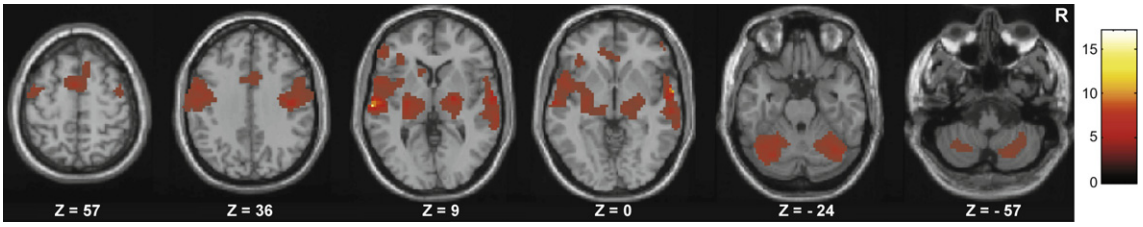

Fig. 2. Hemodynamic main effects (One-way ANOVA) across all syllable categories and subjects displayed on transverse sections of the averaged anatomical reference images (*z*, distance to the intercommisural plane; R, right hemisphere).

the cerebellar hemispheres (lobule VIII; Schmahmann, Doyon, Toga, Petrides, & Evans, 2000). In addition, a rather small hemodynamic activation spot emerged within the vermis of the cerebellum. Anterior insula, IFG, and the caudatum showed an exclusively left-sided response, at the given threshold level, whereas a bilateral, but often predominantly left-sided distribution of the remaining hemodynamic main effects could be noted. Whereas the IFG activation peak was found to be localized within Brodmann area (BA) 45, this activation cluster widely encroached in caudal direction upon BA 44. Therefore, this main effect is assigned to the "posterior IFG".

3.2.2. Cognitive subtraction procedures

Comparison of the hemodynamic responses to complex and simple syllables (CCV versus CV) revealed left-hemisphere activation of the anterior insula, ipsilateral IFG, and the inferior cerebellum (lobule VIII) of both sides (Fig. 3, upper panels). The reversed contrast (comparison of simple and complex syllables = CV versus CCV) as well as the analysis of frequency main effects (LF versus HF and vice versa) did not yield any significant effects. As compared to the complexity main effect, the calculation of the contrast CCV/LF versus CV/HF syllables delineated a nearly identical network, again encompassing left-sided IFG, ipsilateral anterior intrasylvian cortex, and lobule

Table 1
Hemodynamic main effects and cognitive subtractions

		Main effect (across all categories)	Subtraction analysis (complex versus simple syllables)	Subtraction analysis (complex/low-frequency syllables versus simple/high-frequency syllables)
Supplementary motor area (SMA)	Left	4.94 [−6 3 57]	n.s.	n.s.
Motor/somato-senosry cortex	Left	6.45 [−48 −6 36]	n.s.	n.s.
	Right	5.43 [48 −6 33]	n.s.	n.s.
Inferior frontal gyrus (IFG)	Left	5.52 [−51 39 9]	4.37 [−54 36 9]	5.20 [−54 39 12]
Superior temporal gyrus	Left	6.59 [−57 −9 6]	n.s.	n.s.
	Right	3.98 [54 −18 9]	n.s.	n.s.
Anterior insula	Left	4.86 [−36 15 0]	3.89 [−33 18 3]	4.30 [−36 15 3]
Putamen/pallidum	Left	7.88 [−27 −3 0]	n.s.	n.s.
	Right	5.98 [24 −3 3]	n.s.	n.s.
Caudatum	Left	4.02 [−12 15 9]	n.s.	n.s.
Thalamus	Left	7.14 [−15 −18 6]	n.s.	n.s.
	Right	4.88 [18 −21 3]	n.s.	n.s.
Superior cerebellum	Left	5.19 [−21 −60 −24]	n.s.	n.s.
	Right	7.93 [24 −60 −24]	n.s.	n.s.
Inferior cerebellum	Left	5.84 [−21 −60 −57]	7.91 [−24 −63 −51]	9.79 [−24 −63 −51]
	Right	9.43 [18 −63 −57]	10.47 [27 −66 −48]	13.77 [24 −66 −51]

Note. T values represent the activation maximum within each region. SPM coordinates are printed in square brackets.

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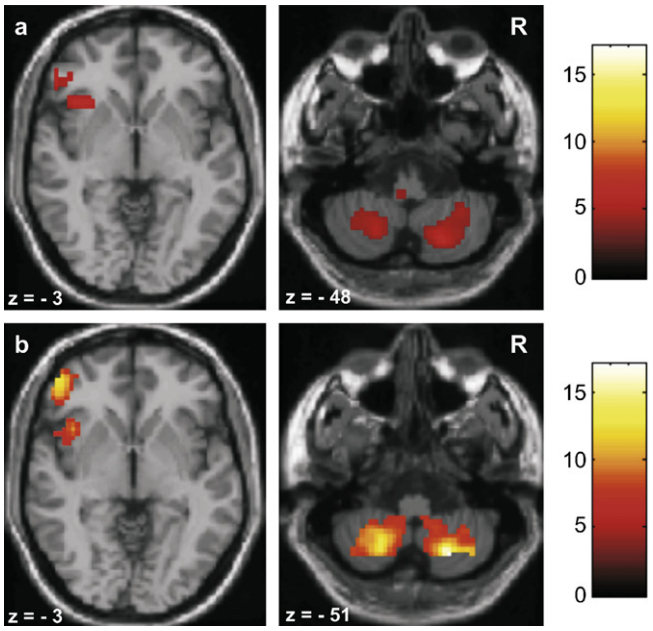

Fig. 3. Cognitive subtraction analysis (One-way ANOVA). (a) Complex versus simple syllables; (b) complex low-frequency (CCV/LF) versus simple high-frequency (CV/HF) syllables. fMRI activation patterns are displayed on transverse sections of the averaged anatomical reference image across all subjects (calculated in arbitrary units by SPM5; R, right hemisphere; *z*, distance to the intercommisural plane).

VIII of both cerebellar hemispheres, characterized, however, by clearly enhanced maximum BOLD signal effects (Fig. 3, lower panels). The remaining subtractions, i.e., CCV/HF versus CV/LF, and the two reversed complexity as well as frequency conditions, did not yield any significant effects.

3.2.3. Functional connectivity analysis

Calculation of the correlation coefficients was restricted to the two contrasts associated with significant hemodynamic effects, i.e., CCV versus CV and CCV/LF versus CV/HF, since in the absence of VOIs an extraction of time series of the BOLD signal cannot be performed. Functional connectivity analysis based upon the contrast of CCV versus CV syllables revealed a quite homogeneous distribution of correlation coefficients across the various areas of speech motor control, extending from .61 to .83 (Table 2). In contrast, the comparisons CCV/LF versus CV/HF syllables yielded clearly enhanced correlation coefficients between left anterior insula and left IFG (Table 3).

4. Discussion

4.1. Cerebral correlates of speech motor control

In line with preceding fMRI studies of our group, based on a syllable repetition paradigm (Riecker et al., 2005; Riecker, Kassubek, Gröschel, Grodd, & Ackermann, 2006), the observed pattern of hemodynamic main effects during the production of bisyllabic nonsense words across

Table 2
Standard correlation analysis of the time series of hemodynamic activation (CCV versus CV contrast) in selected volumes of interest (VOI)

	Supplementary motor area	Inferior frontal gyrus	Anterior insula	Superior cerebellum	Inferior cerebellum	Motor cortex	Thalamus	Putamen/ pallidum	Caudatum
Supplementary motor area	**1**	0.690 ± 0.036	0.73 ± 0.035	0.78 ± 0.057	0.72 ± 0.056	0.84 ± 0.043	0.65 ± 0.056	0.71 ± 0.028	0.81 ± 0.129
Inferior frontal gyrus	0.690 ± 0.036	**1**	0.81 ± 0.138	0.61 ± 0.039	0.62 ± 0.050	0.65 ± 0.047	0.67 ± 0.045	0.70 ± 0.038	0.74 ± 0.257
Anterior insula	0.73 ± 0.035	0.81 ± 0.138	**1**	0.69 ± 0.035	0.72 ± 0.041	0.72 ± 0.057	0.83 ± 0.042	0.83 ± 0.041	0.82 ± 0.023
Superior cerebellum	0.78 ± 0.057	0.61 ± 0.039	0.69 ± 0.035	**1**	0.83 ± 0.083	0.67 ± 0.039	0.68 ± 0.029	0.67 ± 0.038	0.76 ± 0.132
Inferior cerebellum	0.72 ± 0.056	0.62 ± 0.050	0.72 ± 0.041	0.83 ± 0.083	**1**	0.83 ± 0.042	0.70 ± 0.071	0.65 ± 0.047	0.78 ± 0.101
Motor cortex	0.84 ± 0.043	0.65 ± 0.047	0.72 ± 0.039	0.67 ± 0.039	0.83 ± 0.042	**1**	0.63 ± 0.055	0.69 ± 0.076	0.68 ± 0.127
Thalamus	0.65 ± 0.056	0.67 ± 0.045	0.83 ± 0.042	0.68 ± 0.029	0.70 ± 0.071	0.63 ± 0.055	**1**	0.77 ± 0.073	0.78 ± 0.065
Putamen/pallidum	0.71 ± 0.028	0.70 ± 0.038	0.83 ± 0.041	0.67 ± 0.038	0.65 ± 0.047	0.69 ± 0.076	0.77 ± 0.073	**1**	0.83 ± 0.101
Caudatum	0.81 ± 0.129	0.74 ± 0.257	0.82 ± 0.023	0.76 ± 0.132	0.78 ± 0.101	0.68 ± 0.127	0.78 ± 0.065	0.83 ± 0.101	**1**

Note. Correlation coefficient and standard deviation of time series in selected volumes of interest. Low correlation ⩽ .5, intermediate correlation ⩽ .7, high correlation ⩽ .9, and very high correlation > .9 (displayed in bold).

Table 3
Standard correlation analysis of the time series of hemodynamic activation (CCV/LF versus CV/HF contrast) in selected volumes of interest (VOI)

	Supplementary motor area	Inferior frontal gyrus	Anterior insula	Superior cerebellum	Inferior cerebellum	Motor cortex	Thalamus	Putamen/ pallidum	Caudatum
Supplementary motor area	**1**	0.77 ± 0.043	0.77 ± 0.071	0.85 ± 0.053	0.87 ± 0.052	0.91 ± 0.042	0.88 ± 0.046	0.85 ± 0.057	0.83 ± 0.163
Inferior frontal gyrus	0.77 ± 0.043	**1**	**0.98 ± 0.145**	0.77 ± 0.036	0.82 ± 0.049	0.77 ± 0.050	0.87 ± 0.042	0.82 ± 0.093	0.85 ± 0.201
Anterior insula	0.77 ± 0.071	**0.98 ± 0.145**	**1**	0.77 ± 0.051	0.82 ± 0.035	0.71 ± 0.047	0.87 ± 0.028	0.83 ± 0.039	0.95 ± 0.041
Superior cerebellum	0.85 ± 0.053	0.77 ± 0.036	0.77 ± 0.051	**1**	0.93 ± 0.065	0.83 ± 0.032	0.87 ± 0.038	0.86 ± 0.093	0.87 ± 0.086
Inferior cerebellum	0.87 ± 0.052	0.82 ± 0.049	0.82 ± 0.035	0.93 ± 0.065	**1**	0.85 ± 0.033	0.92 ± 0.066	0.91 ± 0.039	0.90 ± 0.094
Motor cortex	0.91 ± 0.042	0.77 ± 0.050	0.71 ± 0.047	0.83 ± 0.032	0.85 ± 0.033	**1**	0.84 ± 0.075	0.83 ± 0.056	0.82 ± 0.046
Thalamus	0.88 ± 0.046	0.87 ± 0.042	0.87 ± 0.028	0.87 ± 0.038	0.92 ± 0.066	0.84 ± 0.075	**1**	0.95 ± 0.046	0.92 ± 0.073
Putamen/pallidum	0.85 ± 0.057	0.82 ± 0.093	0.83 ± 0.039	0.86 ± 0.093	0.91 ± 0.039	0.83 ± 0.056	0.95 ± 0.046	**1**	0.92 ± 0.059
Caudatum	0.83 ± 0.163	0.85 ± 0.201	0.95 ± 0.041	0.87 ± 0.086	0.90 ± 0.094	0.82 ± 0.046	0.92 ± 0.073	0.92 ± 0.059	**1**

Note. Correlation coefficient and standard deviation of time series in selected volumes of interest. Low correlation ⩽ .5, intermediate correlation ⩽ .7, high correlation ⩽ .9, and very high correlation > .9 (displayed in bold).

all stimulus categories encompasses the cerebral structures assumed to support, as inferred from clinical data, the generation of phonetic plans (fronto-opercular and intrasylvian cortex) as well as the execution of the respective vocal tract movement sequences (primary sensorimotor cortex, basal ganglia, cerebellum, thalamus). Furthermore, responses of SMA and adjacent ACG could be documented. These structures appear to mediate motivational aspects of verbal behavior and to engage in the initiation of vocal tract activities during speech production (“starting mechanism”; Botez & Barbeau, 1971), since patients suffering from damage to left SMA may exhibit reduced spontaneous verbal behavior, a “flat” intonation and sometimes dysfluent, i.e., stuttering-like behavior, in the absence of any further articulatory/phonatory deficits or any deterioration of language functions (Ackermann & Ziegler, in press). Furthermore, bilateral lesions of mesiofrontal areas, encroaching upon ACG and its projections to SMA, may give rise to the syndrome of akinetic mutism, characterized by a lack of self-initiated motor activities, including speech production (Ackermann & Ziegler, 1995).

The participants of the present study had been asked to read aloud pseudowords displayed via head-mounted video-glasses. It cannot be excluded that manipulation of these test materials in terms of syllable frequency and complexity also affected visual stimulus encoding, preceding speech motor control processes. For example, lexical decision or reading tasks found pseudowords to elicit larger IFG activation than lexical entries (Mechelli, Gorno-Tempini, & Price, 2003; see Price & Mechelli, 2005, for a review). In order to further delineate these eventual confounding effects, subsequent functional imaging studies must compare hemodynamic activation in response to auditory and visual stimulus presentation.

Calculation of the hemodynamic main effects revealed activation of the superior temporal cortex, an area, usually not considered to pertain to the classical speech production network. However, several functional imaging studies have reported hemodynamic reactions of posterior components of the superior temporal gyrus (pSTG) in speech production tasks such as word generation or reading (Price et al., 1996). Furthermore, damage to left-hemisphere pSTG may compromise the phonological structure of verbal utterances (see Hickok, 2001, for a review). Hence, the observed superior temporal responses might reflect the engagement of this area in interfacing perceptual processes and speech production.

Based upon a conjunction analysis of hemodynamic activation (versus baseline) in response to four different trisyllabic sequences, Bohland and Guenther (2006) were able to delineate a “minimal network for overt speech production”. Another recent fMRI study compared the production of vowel /a:/ with a rest condition, in order to identify the cerebral correlates of motor aspects of language production (Sörös et al., 2006). The present study, based upon nonsense words as test materials, yielded a quite similar distribution of hemodynamic activation as

compared to these preceding investigations. However, some minor differences must be noted. By contrast to a rather strictly symmetrical infratentorial response pattern, the investigation by Bohland and Guenther documented predominantly right-sided activity, both within superior and inferior parts of the cerebellum (see Fig. 2 in Bohland & Guenther, 2006). Most presumably, differences in the experimental design account for these effects. Whereas the study by Bohland and Guenther (2006) required subjects to focus upon and keep in mind the written syllables for several seconds each, the participants of the present investigation, by contrast, were instructed to produce the bisyllabic items as soon as possible after visual presentation, a procedure lacking any significant demands upon verbal rehearsal mechanisms. These mechanisms may also engage the cerebellum (Cabeza & Nyberg, 2000). Since essential components of verbal working memory are lateralized towards left frontal and parietal areas, an extra computational load upon the right cerebellar hemisphere can be expected under these conditions, given the reciprocal contralateral cerebro-cerebellar interconnections. As another discrepancy, furthermore, the hemodynamic main effects of the present study did not encompass activation spots within the base of the pons (Bohland & Guenther, 2006) or the nucleus ruber (Sörös et al., 2006). Whereas ventral pontine structures represent a relay station of fronto-cerebellar projections, any contribution of the nucleus ruber to speech motor control awaits further elucidation.

Taken together, a series of functional imaging studies addressing different mechanisms of speech motor control, based either upon syllable repetitions, the production of pseudowords, or isolated vowels, roughly converge upon a "minimal network for overt speech production", including mesiofrontal areas, intrasylvian cortex, pre- and postcentral gyrus, extending rostrally into posterior parts of the left inferior frontal convolution, basal ganglia, cerebellum, and thalamus.

4.2. Impact of syllable complexity and frequency upon the cerebral network of speech motor control

About 500 out of a total of more than 12,000 syllables occurring in languages like German and English suffice to generate ca. 85% of a speaker's verbal utterances. Based upon such observations, Levelt and colleagues (1999) argue that these HF syllables need not be compiled from segmental data structures, but are retrieved as stored programs from a mental syllabary. Besides syntactic rules and word forms, thus, speakers access during speech production a further "knowledge base", consisting of ensembles of highly overlearned articulatory gestures. Based upon this model of a mental syllabary, the "programming" of LF and HF syllables must be expected to be associated with different computational mechanisms. As a consequence, the generation of words containing LF or HF syllables, respectively, might be bound, at least partially, to separate cerebral networks and, therefore, different patterns of brain activation. At variance with this suggestion, computation of the contrast LF versus HF items, calculated across the two levels of syllable onset complexity, did not reveal any significant hemodynamic frequency effects. Conceivably, the difference in processing loads between a syllabic and a sub-syllabic encoding mechanism might be so small that it escapes the resolution power of contemporary functional imaging methods. In fact, the indirect, sub-syllabic encoding route, if it exists, must be almost as efficient as the direct, syllabic route, since only very small reaction time differences between LF and HF syllable production could be found in highly constrained experimental settings and no obvious cleft between HF and LF syllables is recognizable in everyday spoken language. Nevertheless, a rejection of the mental syllabary concept still must be considered premature, since a preceding study reported enhanced activation of the left insula in association with LF as compared to HF syllables, irrespective of word frequency, during reading of lexical items (Carreiras et al., 2006). And a series of investigations documented a robust syllable frequency effect in Spanish speakers (Carreiras & Perea, 2004; Carreiras, Vergara, & Barber, 2005; Perea, Rosa, & Gómez, 2005), although differences in stimulus type (words versus pseudowords) might at least partly account for the differences between HF and LF items in these studies. Furthermore, it is not clear whether the Spanish test materials were controlled for syllable structure. As an indication of some impact of syllable frequency upon cerebral hemodynamic activation, the present investigation found an interaction between frequency and onset complexity. The contrast CCV/LF versus CV/HF syllables gave rise to enhanced responses of the structures susceptible to syllable onset complexity, i.e., left-hemisphere posterior IFG/anterior insula and both cerebellar hemispheres. These results point at substantially enhanced processing requirements in case of complex-LF syllables: this particular group of items might, on the basis of their low-frequency of occurrence, require sub-syllabic encoding, and, as a consequence of their complex structure, pose additional computational demands upon phonetic planning.

Contrary to expectation, a main effect of syllable onset complexity (CCV versus CV), calculated across the two frequency categories HF and LF, emerged, characterized by a hemodynamic response of posterior IFG and the anterior insula of the language-dominant hemisphere, concomitant with bilateral activation of the cerebellar hemispheres. Assuming left fronto-opercular and intrasylvian cortex to participate in speech motor planning, this process appears to be sensitive to the phonetic/phonological complexity of syllable structure.

Considering that the brain lesions of AOS patients commonly involve the above structures, this result helps to explain why complex syllables are particularly challenging to patients with AOS (Staiger & Ziegler, in press). In addition, the observed complexity effect has a significant impact upon models of the functional architecture of phonetic encoding mechanisms: A frequency-independent hemody-

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namic main effect of complexity within areas devoted to pre-articulatory mechanisms of speech production argues against the view that syllable-sized phonetic representations are processed as holistic units in speech production. Within the framework of Levelt's theory, variation of onset complexity should have no impact on the production of HF syllables, since both simple and complex HF units should be represented by precompiled motor plans (see above). Instead, the current results suggest that, even in case of HF syllables, the sub-syllabic details of articulation require additional computational resources, which are provided by ventral parts of the dorsolateral frontal cortex of the language-dominant hemisphere. Functional imaging studies found these areas also to be engaged in speech perception, i.e., the segmentation of syllable onsets during the discrimination of word pairs (Burton, Small, & Blumstein, 2000). Thus, the left anterior perisylvian cortex appears to support the processing of the fine-grained sound structure of verbal utterances on a broader scale, perhaps as an extension of the sequential speech motor capacities of left motor and premotor cortical and insular cortex.

Similar to a preceding investigation (Bohland & Guenther, 2006), the subjects of the present study were asked to read visually displayed test materials. Studies of visual word processing, based upon lexical decision or reading tasks, reported enhanced activation of the IFG in association with the processing of pseudowords as compared to lexical entries (Mechelli et al., 2003; Price & Mechelli, 2005, for review). One might speculate, thus, that the hemodynamic main effect of the contrast CCV versus CV at the level of posterior IFG simply reflects the impact of higher visual load (more graphemic information of the CCV items). However, auditory application of words also yields a complexity effect (four- versus monosyllabic lexical items) of the anterior perisylvian cortex (Shuster & Lemieux, 2005). Apart from these data, activation of IFG has been observed in a variety of tasks lacking any visual input, e.g., (syntactically specialized) working memory (Santi & Grodzinsky, 2007), motor imitation (Iacoboni & Wilson, 2006), or the segmentation of speech and nonspeech sound sequences (Burton et al., 2000; Burton & Small, 2006). Nevertheless, we cannot completely exclude that the observed activation of IFG can be attributed to mechanisms other than speech motor control. As an alternative, IFG might be involved in the generation of the input of the feed-forward model, engaged in the planning of articulatory sequences (Iacoboni & Wilson, 2006).

Based upon clinical findings in ataxic dysarthria as well as functional imaging data obtained from healthy subjects, the cerebellum has been assumed to support the concatenation of canonical templates retrieved from the mental syllabary into a fully parsed inner speech code (Ackermann, Mathiak, & Ivry, 2004a; Ackermann, Mathiak, & Riecker, 2007). Thus, the observed network of supratentioral fronto-opercular/intrasylvian areas and infratentorial cerebellar structures, as delineated by the contrast of CCV versus CV syllables, might reflect the cooperation of these structures at a pre-articulatory level of speech motor control. Considering the findings of the present experiment, however, the cerebellum appears to participate not only in syllable sequencing, but also in the processing of sub-syllabic phonetic units. By contrast, sensorimotor cortex, thalamus, and the basal ganglia did not show a significant increase of the BOLD signal. At a first glance, CCV syllables should pose higher demands on motor execution mechanisms than CV items. For example, the production of a CCV cluster like /kla/ requires more elaborate tongue manoeuvres than /ka/, i.e., an additional excursion of the tip of the tongue. At variance with this expectation, production of complex (versus simple) syllable onsets was found to pose additional control demands upon the motor planning rather than the execution apparatus. Apparently, once the respective sequences of vocal tract movements have been "programmed", the subsequent generation of the output of primary motor cortex, involving cortico-striatal loops, is more or less comparable across the syllable types examined in this study.

Most studies addressing the impact of articulatory/phonetic task demands upon hemodynamic brain activation contrasted multi- and mono-syllabic items, i.e., evaluated the sequencing of syllable strings (Riecker et al., 2000; Shuster & Lemieux, 2005). The concatenation of sub-syllabic phonetic units has found less attention so far. Comparing tri-syllabic CC(C)V-CC(C)V-CC(C)V sequences with CV-CV-CV items, a preceding fMRI study found higher syllable complexity to be associated with a more extended pattern of hemodynamic responses, including pre-SMA and the opercular/insular junction of both hemispheres, left-sided parietal cortical areas, and right superior cerebellum (Bohland & Guenther, 2006). As already noted, this latter experiment posed considerable demands upon verbal working memory. Thus, enhanced left-parietal hemodynamic reactions might reflect the higher load of the phonological store in association with CC(C)V-sequences.

Bohland and Guenther (2006) used three-syllabic utterances as test materials. As a consequence, increased recruitment of mechanisms subserving the initiation and continuous flow of speech may have been implicated. Such mechanisms have often been associated with functions of the SMA. Hence, mesiofrontal activation as found by these authors is not unexpected. In an experimental study of a patient with a hemorrhagic lesion undercutting SMA, Ziegler, Kilian, and Deger (1997) found substantially increased reaction times to three-syllabic as compared to two-syllabic nonwords, whereas the phonetic content of the syllables to be produced had no impact on this measure. In AOS patients, on the contrary, a reverse reaction time effect was observed by Deger and Ziegler (2002): These patients' vocal reaction times were sensitive to the phonetic content of disyllabic utterances, but not to syllable number. Thus, SMA appears to operate as a pacing device which supplies the syllabic "frames" of an utterance (McNeilage, 1998), whereas the structures affected in AOS,

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i.e., left posterior IFG and/or left anterior insular cortex, seem to be more concerned with the programming of the phonetic "content" of these frames. The test materials of the present experiment might have failed to elicit hemodynamic SMA responses because they impose higher demands on the lateral "content"-than on the medial "frame"-system.

4.3. Functional connectivity of fronto-opercular and intrasylvian cortex

The calculation of the correlation coefficients between the time series of BOLD signal changes has proved a valuable tool for the analysis of the cerebral correlates of syllable repetitions synchronized to click trains (Riecker et al., 2005). Analysis of the temporal dynamics of cerebral hemodynamic responses revealed, under these conditions, that the various cortical and subcortical brain regions engaged in speech motor control are organized into two networks: very high correlations (coefficient > .9) emerged between left SMA, left anterior insula, left dorsolateral frontal cortex, including Broca's area, as well as superior cerebellum, on the one hand, and between sensorimotor cortex, thalamus, putamen/pallidum, left caudatum and inferior cerebellum, on the other. In consideration of the time course of hemodynamic activation, these two loops were assigned to the preparation/initiation and the execution, respectively, of vocal tract activity during speech production. At least during syllable repetitions, thus, ventral premotor and intrasylvian cortex of the left hemisphere appear to operate in concert. However, this design cannot be expected to pose any significant demands upon phonetic sequencing mechanisms and, therefore, might provide limited insights into the contribution of Broca's area and anterior insula to speech motor control. For example, the strong correlation between SMA, posterior IFG, intrasylvian cortex, and superior cerebellum might simply reflect the generation of a predictive timing signal, i.e., the implementation of a clock mechanism within the vocal domain. Functional connectivity analysis of the production of nonsense words, in the present study, yielded quite different results. Based upon the CCV versus CV contrast, no distinct pattern of correlation coefficients emerged. Comparison of the time series of the BOLD signal of posterior IFG and anterior insula yielded a value of only .81. However, this parameter leaped to .98 for the contrast CCV/LF versus CV/HF items. Several other correlations showed comparable changes, e.g., SMA and motor cortex or various components of the basal ganglia. In these regions of interest, however, enhanced functional connectivity was not paralleled by a significant increase of hemodynamic activation. As a consequence, modulation of focal responses, on the one hand, and changes in functional connectivity within the "minimal network for overt speech production", on the other, seem to represent two at least partially independent organizational principles of the brain to efficiently master speech motor tasks. And the latter mechanism might support the higher computational demands associated with LF syllables.

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Appendix. Pseudowords used in the fMRI-experiment

High-frequent/ simple (hs)			High-frequent/ complex (hc)			Low-frequent/ simple (ls)			Low-frequent/ complex (lc)		
	L	P		L	P		L	P		L	P
dahtet	6	5	blietet	7	6	dühtet	6	5	drautet	7	6
dehtet	6	5	dreitet	7	6	föhtet	6	5	frähtet	7	6
gietet	6	5	frietet	7	6	fuhtet	6	5	frohtet	7	6
guhtet	6	5	frahtet	7	6	geitet	6	5	grehtet	7	6
kahtet	6	5	frühtet	7	6	geutet	6	5	greutet	7	6
lehtet	6	5	grohtet	7	6	huhtet	6	5	gnühtet	7	6
mahtet	6	5	klahtet	7	6	kähtet	6	5	krohtet	7	6
mehtet	6	5	krietet	7	6	lähtet	6	5	plähtet	7	6
mohtet	6	5	trahtet	7	6	mautet	6	5	pleutet	7	6
nehtet	6	5	trietet	7	6	pautet	6	5	plohtet	7	6
neutet	6	5	spietet	7	6	peutet	6	5	schleutet	9	6
pohtet	6	5	zahtet	6	6	pühtet	6	5	stautet	7	6
tietet	6	5	zietet	6	6	sautet	6	5	truhtet	7	6
wietet	6	5	zohtet	6	6	seutet	6	5	zautet	6	6
fohtet	*6*	*5*	*grühtet*	*7*	*6*	*keutet*	*6*	*5*	*klöhtet*	*7*	*6*
meitet	*6*	*5*	*zuhtet*	*6*	*6*	*pöhtet*	*6*	*5*	*prehtet*	*7*	*6*

L, number of letters; P, number of phonemes; the last two items of each column were repeated three times each per run.

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