

Cerebral pathways in processing of affective prosody: A dynamic causal modeling study

Thomas Ethofer,^{a,b,*} Silke Anders,^{a,b} Michael Erb,^a Cornelia Herbert,^c Sarah Wiethoff,^{a,b}
Johanna Kissler,^c Wolfgang Grodd,^a and Dirk Wildgruber^b

^aSection of Experimental MR of the CNS, Department of Neuroradiology, Otfried-Mueller-Strasse 51,
University of Tuebingen, 72076 Tuebingen, Germany

^bDepartment of General Neurology, Hertie-Institute for Clinical Brain Research, University of Tuebingen, Tuebingen, Germany

^cDepartment of Psychology, University of Konstanz, Konstanz, Germany

Received 19 May 2005; revised 5 August 2005; accepted 19 September 2005
Available online 4 November 2005

This study was conducted to investigate the connectivity architecture of neural structures involved in processing of emotional speech melody (prosody). 24 subjects underwent event-related functional magnetic resonance imaging (fMRI) while rating the emotional valence of either prosody or semantics of binaurally presented adjectives. Conventional analysis of fMRI data revealed activation within the right posterior middle temporal gyrus and bilateral inferior frontal cortex during evaluation of affective prosody and left temporal pole, orbitofrontal, and medial superior frontal cortex during judgment of affective semantics. Dynamic causal modeling (DCM) in combination with Bayes factors was used to compare competing neurophysiological models with different intrinsic connectivity structures and input regions within the network of brain regions underlying comprehension of affective prosody. Comparison on group level revealed superiority of a model in which the right temporal cortex serves as input region as compared to models in which one of the frontal areas is assumed to receive external inputs. Moreover, models with parallel information conductance from the right temporal cortex were superior to models in which the two frontal lobes accomplish serial processing steps. In conclusion, connectivity analysis supports the view that evaluation of affective prosody requires prior analysis of acoustic features within the temporal and that transfer of information from the temporal cortex to the frontal lobes occurs via parallel pathways.

© 2005 Elsevier Inc. All rights reserved.

Keywords: Connectivity; Dynamic causal modeling; Emotion; Non-verbal; Prosody

Introduction

In spoken language, information about the emotional state of the speaker can be expressed via propositional cues at the verbal level and via non-verbal means of communication by modulation of the speech melody (affective prosody). Affective prosody is characterized by variations of suprasegmental language features, such as pitch, syllable duration, and voice quality (Banse and Scherer, 1996). Evidence obtained from lesion studies indicates a right-hemispheric superiority in processing of these features (Blonder et al., 1991; Bowers et al., 1987; Borod et al., 2002). In line with this suggestion, functional imaging studies have consistently demonstrated right-lateralized activations at the level of the auditory cortex during evaluation of affective prosody (Mitchell et al., 2003; Wildgruber et al., 2005). However, it has been shown that left-hemispheric lesions can also compromise comprehension of affective speech melody (Adolphs et al., 2002; Hornak et al., 1996, 2003; Kucharska-Pietura et al., 2003; Pell, 1998; van Lancker and Sidtis, 1992) challenging the hypothesis that processing of affective prosody is exclusively subserved by the right hemisphere. Specifically, unilateral lesions within the inferior frontal cortex of both hemispheres as well as deep white matter lesions of the mid-rostral part of the corpus callosum can result in severe deficits in comprehension of affective prosody (Hornak et al., 1996, 2003; Ross et al., 1997). Accordingly, functional neuroimaging and event-related electrophysiological studies on the neural correlates underlying the comprehension of affective prosody demonstrated bilateral activations in the inferior frontal lobe (Imaizumi et al., 1997; Pihan et al., 2000; Wildgruber et al., 2002, 2004). These converging results from lesion and neuroimaging studies suggest that the frontal lobes of both hemispheres cooperate in decoding of non-verbal emotional information in the voice and that intact transcallosal communication of information is necessary for comprehension of affective prosody. However, neither lesion studies nor conventional analysis of functional imaging data can

* Corresponding author. Section of Experimental MR of the CNS, Department of Neuroradiology, Otfried-Mueller-Strasse 51, University of Tuebingen, 72076 Tuebingen, Germany. Fax: +49 7071 294371.

E-mail address: Thomas.Ethofer@med.uni-tuebingen.de (T. Ethofer).

Available online on ScienceDirect (www.sciencedirect.com).

clarify whether this cooperation of both hemispheres is accomplished in a serial way via sequential processing steps or if both frontal lobes receive their information independently from each other from the right temporal cortex. It was the aim of this study to investigate the connectivity pattern subserving communication between the right temporal cortex and the frontal lobes during decoding of affective prosody. To this end, we used event-related functional magnetic resonance imaging (fMRI) combined with the novel technique of dynamic causal modeling (Friston et al., 2003). Dynamic causal modeling enables inferences on (1) the parameters representing influences of experimentally designed inputs, (2) the intrinsic coupling of different brain regions, and (3) how this coupling is modulated by an experimental factor. Given the lack of knowledge on the connectivity between neural areas implicated in processing of affective prosody, we precluded modulating factors and focused on the investigation of input regions and the intrinsic connectivity pattern within this network. Therefore, we compared models in which the right secondary auditory cortex serves as input region with models in which direct inputs are assumed to enter the network via one of the frontal areas. Furthermore, to investigate the architecture of the interregional connections, we compared dynamic causal models corresponding to serial and parallel processing within the frontal lobes.

Material and methods

Subjects

24 right-handed German native speakers (11 males, 13 females, mean age 24.4 years) with no history of neurological or psychiatric illness participated in an fMRI experiment. Handedness was determined using the Edinburgh Inventory (Oldfield, 1971). The Ethical Committee of the University of Tuebingen had approved the investigation. Informed consent was obtained according to the Declaration of Helsinki.

Stimuli

Six professional actors (3 females/3 males) pronounced 162 German adjectives in either happy, neutral, or angry intonation (54 for each intonation). The adjectives were selected from a pool of 500 adjectives on the basis of ratings obtained from 45 healthy German native speakers (Herbert et al., submitted for publication) who judged these words after visual presentation on a 9-point self assessment manikin scale (SAM, Bradley and Lang, 1994) along the dimensions of valence (ranging from 1 = highly positive to 9 = highly negative) and arousal (ranging from 1 = very calming to 9 = highly arousing). The stimulus set comprised 54 highly arousing positive (mean arousal rating > 4, mean valence rating < 4, e.g. “verführerisch” [alluring]), 54 highly arousing negative (mean arousal rating > 4, mean valence rating > 6, e.g. “panisch” [panic]), and 54 low arousing neutral (mean arousal rating < 4, mean valence rating between 4 and 6, e.g. “breit” [broad]). Low arousing neutral adjectives were preferred over high arousing ones, since they more clearly represented neutral semantic valence, while high arousing words with a mean valence rating between 4 and 6 were ambiguous in many cases (e.g. “skurril” [cranky]) and rated as either positive or negative by the majority of subjects.

To ensure that judgment of emotional word content is comparable between visual and auditory presentation and to

evaluate the valence of the non-verbal information, these stimuli were presented acoustically to 42 healthy German native speakers (mean age 28.8, 21 males, 21 females) in a prestudy comprising two sessions with 81 trials each. Volunteers were instructed to judge in one session the valence of the emotional word content and the valence of the affective prosody in the other session. The order of tasks was pseudorandomized across subjects. Mean group ratings of emotional word content during visual and auditory presentation of the stimuli were strongly correlated ($r = 0.98$) indicating that judgment of emotional semantics is comparable across modalities. Mean valence ratings of affective prosody were 3.3 ± 0.2 for happy intonations, 5.4 ± 0.1 for neutral intonations, and 6.6 ± 0.2 for angry intonations (mean \pm standard error) indicating that the participants recognized the emotional valence intended by the actors.

Experimental design

The fMRI experiment consisted of two sessions (40 and 41 trials, respectively) in which subjects judged the valence of emotional word content and two sessions (40 and 41 trials, respectively) where subjects were to rate the valence of the affective prosody. Stimuli were balanced over tasks with respect to valence of word content (5.0 ± 0.2 and 5.0 ± 0.2), arousal of word content (4.7 ± 0.1 and 4.5 ± 0.1), valence of affective prosody (4.9 ± 0.2 and 5.2 ± 0.2), and word frequency in written (38.4 ± 9.9 and 40.0 ± 9.9) and spoken (5.5 ± 3.1 and 5.9 ± 1.9) language as assessed by the Mannheim Corpus of the Institut für Deutsche Sprache, Mannheim (all values in mean \pm standard error). Stimuli were presented binaurally via magnetic resonance-compatible headphones with piezoelectric signal transmission (Jäncke et al., 2002). The order of stimulus presentation was randomized within sessions and the order of sessions and tasks was pseudorandomized over subjects. Stimulus onset was jittered relative to the scan onset in steps of repetition time (TR)/4 resulting in intertrial intervals ranging from 20.3 to 24.9 s (9–11 TRs). Rating was performed on a 9-point SAM scale which was shown for 4 s, 200 ms after stimulus offset (see Fig. 1). Subjects conveyed their decision via a fiber optic system which allowed them to move a white dot on the SAM scale leftwards or rightwards by pressing the corresponding buttons in their right or left hand. To avoid lateralization effects caused by motor responses, the arrangement of the symbols of the SAM scale was flipped in horizontal direction for half of the participants of the fMRI experiment.

Image acquisition

Functional and structural images were acquired using a 1.5 T-whole body scanner (Siemens AVANTO, Erlangen, Germany). T_1 -weighted high-resolution ($1 \times 1 \times 1$ mm) structural images were obtained using a magnetization prepared rapid acquisition gradient echo (MPRAGE) sequence. Functional images were acquired by using a multislice echo planar imaging (EPI) sequence covering the whole cerebrum (25 axial slices acquired in descending direction, 4 mm slice thickness, 1 mm gap, TR = 2.26 s, echo time (TE) = 52 ms, flip angle 90° , field of view (FOV) = 192×192 mm², 64×64 matrix, bandwidth 1594 Hz/Px). To enable offline correction of distortions of the EPI images, a static field map (TR = 487 ms, TE = 5.28, and 10.04 ms) was acquired in all subjects prior to the functional measurements.

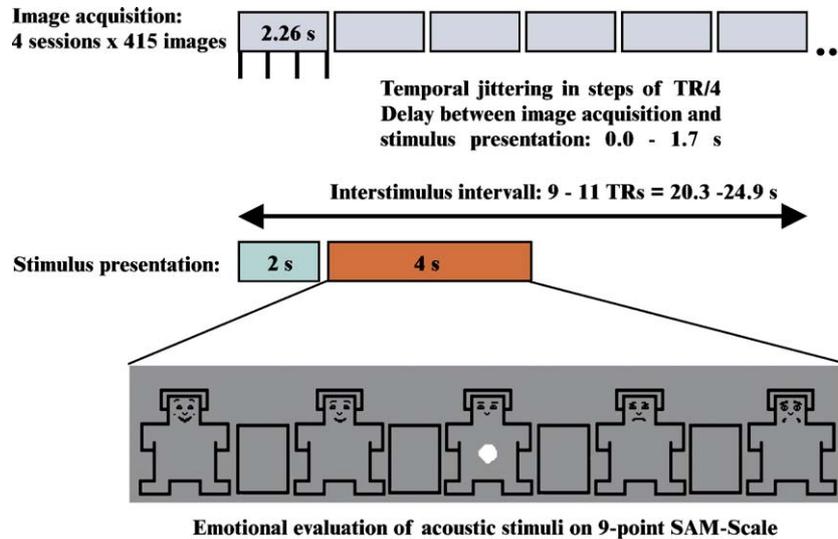


Fig. 1. Experimental setup. Tasks for evaluation of affective prosody and affective semantics were carried out in randomized order across four imaging sessions comprising 415 EPI images. Stimuli were presented via headphones in intervals ranging from 20.3 to 24.9 s. Rating of emotional valence was done on a 9-point SAM scale which was shown for 4 s, 200 ms after stimulus offset.

Conventional image analysis

The first five EPI images of each session were discarded from further analysis in order to exclude measurements preceding T_1 equilibrium. Imaging data were analyzed using statistical parametric mapping software (SPM2, Wellcome Department of Cognitive Neurology, London, UK). Preprocessing of functional images included motion correction, unwarping by use of a static field map, slice time correction to the middle slice, normalization into MNI space (Montreal Neurological Institute, Collins et al., 1994), and spatial smoothing with a Gaussian Filter (10 mm full width half maximum). Statistical analysis relied on a general linear model. Events were time-locked to onset of stimulus presentation and regressors were defined as stick-function convolved with the hemodynamic response function. To correct for low-frequency components, a high-pass filter with a cutoff frequency of 1/128 Hz was used. Serial autocorrelations of fMRI data were accounted for by modeling an autoregressive process with a coefficient of 0.2 (Friston et al., 2002). Task-specific activations were obtained by contrasting hemodynamic responses during judgment of affective prosody and emotional word content. Statistical evaluation of group data was based on second-level random effects analysis with a height threshold of $P < 0.005$ and an extent threshold of $P < 0.05$ (corresponding to a minimal cluster size of 50 voxels), corrected for multiple comparisons within the volumes of interest. Volumes of interest comprised the right middle temporal gyrus and bilateral inferior/middle frontal cortices, and were selected on the basis of lesion (Hornak et al., 2003) and fMRI studies (George et al., 1996; Imaizumi et al., 1997; Buchanan et al., 2000; Mitchell et al., 2003; Wildgruber et al., 2002, 2004, 2005) and defined with the automatic anatomical labeling tool integrated in SPM (Tzourio-Mazoyer et al., 2002).

Dynamic causal modeling

Definition of brain regions included in the dynamic causal models relied on activation clusters obtained from conventional analysis of group data (rating of affective prosody > rating of emotional word content). To allow for interindividual differences

in peak brain activation, time series, which were corrected for nuisance variables, were extracted from a spherical volume (6 mm radius) centered at the most significant voxel within each cluster in individual spmT-maps (rating of affective prosody > rating of emotional word content).

As signal dropouts can compromise estimation of coupling parameters in a way that afferent coupling parameters are overestimated, while efferents from the affected area decrease (Friston et al., 2003), mean intensities within these regions were calculated from normalized mean EPI images to determine whether the selected regions were affected by signal drop outs.

First, we wanted to determine which of the regions defined by the conventional fMRI analysis is the most likely input region. We assumed that external inputs enter the network via the activation cluster within the right temporal cortex. To test this hypothesis formally, models with no a priori constraints on their interregional connectivity structure (fully connected models) in which extrinsic driving inputs were specified for the cluster within the temporal cortex were compared with fully connected models in which one of the other regions found active in the subtraction analysis served as input region.

Second, we wanted to investigate the intrinsic connectivity pattern of regions involved in processing of affective prosody given the input region as determined by the first analysis. To this end, four dynamic causal models (DCMs) with different intrinsic connectivity patterns were constructed: a model with parallel forward connections from the input region to both frontal regions (Model 1), two serial models with the input region as starting point (Models 2 and 3), and a model in which all regions are connected bidirectionally with each other (Model A).

Model evidence (likelihood of the data y given the model m , $P(y|m)$) which is a function of the models accuracy and its complexity was computed based on Bayesian and Akaike information criterion (BIC and AIC, respectively). For model comparison of models $m = 1$ and $m = 2$, Bayes factors B_{12} were calculated for each subject and session by

$$B_{12} = \frac{P(y|m=1)}{P(y|m=2)}. \quad (1)$$

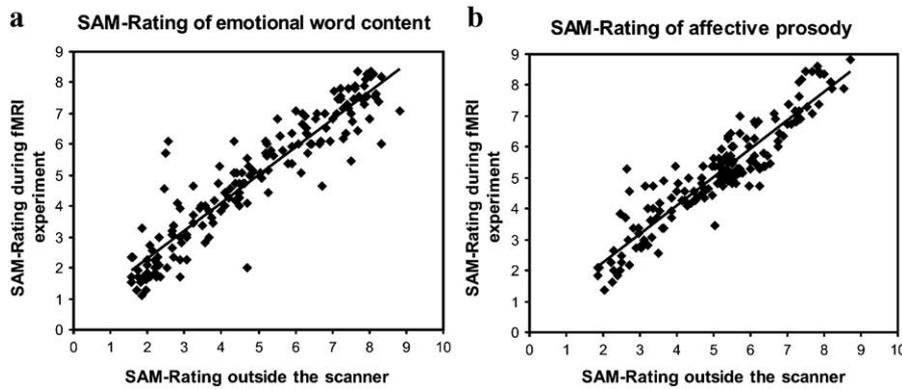


Fig. 2. Behavioral data. Ratings obtained during the fMRI experiment were strongly correlated with ratings obtained in the prestudy for both emotional word content ($r = 0.93$), as well as affective prosody ($r = 0.93$).

Bayes factors > 1 favor Model 1 over Model 2, while Bayes factors < 1 indicate superiority of Model 2 over Model 1. Consistent evidence for superiority of one model over another can be assumed if Bayes factors calculated by use of both AIC and BIC are bigger than e or smaller than $1 / e$ (for detailed description, see Penny et al., 2004). Model evidence was calculated separately for each session and Bayes factors obtained for the two sessions were multiplied with each other. One possibility to perform group analysis over n subjects is to multiply Bayes factors which account for the parametric aspects of the model evidence acquired for each subject:

$$B_{12} = B_{12}(\text{subject } 1) * B_{12}(\text{subject } 2) * \dots * B_{12}(\text{subject } n). \quad (2)$$

However, this procedure is vulnerable to outliers and might, in the worst case, result in inferences which are based on the data of one single subject. Therefore, we additionally employed a non-parametric approach, in which the probability to obtain j or more Bayes factors > 1 in n subjects under the null hypothesis $H_0: P(y | m = 1) = P(y | m = 2)$ can be calculated by:

$$P(X \geq j | H_0) = \sum_{k=j}^n \binom{n}{k} * 0.5^n \quad (3)$$

where X represents a binomially distributed random variable. For comparison of parallel and serial models, the alternative hypothesis $H_1: P(y | m = 1) \neq P(y | m = 2)$ was accepted, if $P(X \geq j | H_0) < 0.025$ for both Bayes factors computed by use of BIC and AIC (two-sided test). A model with plausible intrinsic connectivity structure should explain the data with a higher efficacy than a fully connected model (Model A). Therefore, parallel and serial models were also compared to Model A. For these comparisons, a directional null hypothesis: $H_0: P(y | m = 1) \leq P(y | m = 2)$ was available. Thus, the alternative hypothesis $H_1: P(y | m = 1) > P(y | m = 2)$ was accepted, if $P(X \geq j | H_0) < 0.05$ (one-sided test).

Results

Behavioral data

Mean group ratings of acoustic stimuli in the prestudy and mean group ratings during fMRI were strongly correlated for both emotional word content ($r = 0.93$) and affective prosody ($r = 0.93$) indicating that the participants of the fMRI experiment did

comprehend verbal and non-verbal affective information in presence of scanner noise with sufficient accuracy (see Fig. 2).

Conventional fMRI analysis

To identify brain regions specifically contributing to the processing of affective prosody and emotional word content, blood oxygen level dependent (BOLD) responses during the two tasks were contrasted. By using this subtraction approach, activations within the right posterior temporal cortex (middle temporal gyrus/superior temporal sulcus) and bilateral frontal cortex (middle/inferior frontal gyrus) could be ascribed to the identification of affective prosody. For identification of emotional word content, activations were found in the left anterior temporal lobe, left orbitofrontal gyrus, and left superior frontal gyrus (see Table 1, Fig. 3).

Dynamic causal modeling

Mean signal intensity in the network identified for processing of affective prosody, was 539 ± 11 , 553 ± 6 , and 550 ± 7 in the right posterior middle temporal gyrus, and right and left middle/inferior frontal cortex, respectively (mean \pm standard error, arbitrary units).

Table 1

Task-specific activations during evaluation of affective prosody and emotional semantics

Anatomical definition	Brodman area	MNI coordinates	Z score	Cluster size
<i>Affective prosody > emotional word content</i>				
Left middle/inferior temporal gyrus	45/46	-36 42 6	3.95	141*
Right middle/inferior temporal gyrus	45/46	39 42 6	3.54	94*
Right middle temporal gyrus	21	66 -42 3	3.17	56*
<i>Emotional word content > affective prosody</i>				
Left medial superior frontal gyrus	8/9	-21 36 51	3.80	57
Left temporal pole/middle temporal gyrus	20/21/38	-48 9 -39	3.68	132
Left orbitofrontal gyrus	45/47	-48 30 -6	3.18	91

* $P < 0.05$, corrected for multiple comparisons within predefined volumes of interest.

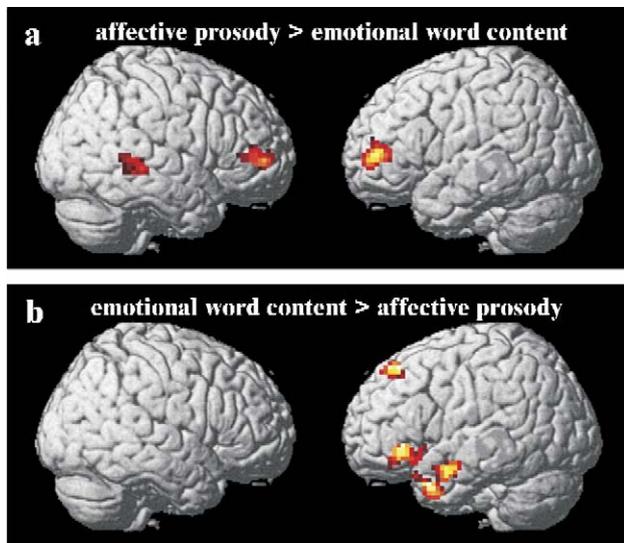


Fig. 3. Task-specific responses during evaluation of affective prosody (a) and emotional semantics (b). Contrasting BOLD responses elicited by the two tasks yielded stronger activations in the right posterior temporal cortex (BA 21) and bilateral middle/inferior frontal gyrus (BA 45/46) during rating of affective prosody, while rating of emotional semantics was associated with stronger responses in the left temporal pole (BA 20/21/38), left lateral orbitofrontal gyrus (BA 45/47), and superior medial frontal gyrus (BA 8/9).

Fully connected dynamic causal models with activation clusters within the right temporal cortex as input region were superior to fully connected alternative models in which one of the activation clusters within the frontal lobe was defined as input region (both group Bayes factors as calculated by Eq. (2) $> 1.80 \times 10^{308}$, both binomial P values as calculated by Eq. (3) < 0.05). This is in agreement with results from the conventional analysis demonstrating a stronger correlation between the stimulus function and the BOLD signal (prosody $>$ baseline) in the right temporal cluster ($T(23) = 7.53$) than in the two frontal clusters ($T(23) = 6.76$ and 6.45 for the left and right frontal area, respectively). To investigate the intrinsic connectivity pattern within this network, dynamic causal models assuming parallel (Model 1), serial (Model 2 and 3), or full connectivity pattern (Model A) were compared (see Fig. 4). Model comparisons on the basis of group Bayes factors as calculated by Eq. (2) and binomial P values as determined by Eq. (3) are given in Table 2. Model 1 in which parallel projection from the posterior middle temporal gyrus to the frontal cortical regions was assumed was significantly superior to both serial models (both group Bayes factors $> 6.66 \times 10^{10}$, both binomial P values < 0.025) as well as the model with fully connected brain regions (group Bayes factor $> 6.66 \times 10^{204}$, binomial P value < 0.05). In a post hoc analysis, we tried to optimize Model 1 by adding either unidirectional or bidirectional connections between the two frontal regions or adding unilateral or bilateral backward projections from the frontal areas to the right posterior middle temporal cortex. Model 1 was significantly superior to all these alternative models (all group Bayes factors $> 3.80 \times 10^{45}$, all binomial P values < 0.025).

Discussion

In the present study, conventional analysis of fMRI data based on a general linear model was employed to identify brain regions

underlying understanding of affective prosody and emotional word content. Subsequently, dynamic causal modeling (Friston et al., 2003) was used to investigate input regions and architecture of interregional connections within the network involved in comprehension of affective prosody.

Cortical networks subserving the perception and understanding of affective prosody

By using a subtraction analysis, the right posterior middle temporal gyrus and bilateral frontal regions were found to be specifically involved in processing of affective prosody. A rightward lateralization of brain responses within the auditory association cortex is in accordance with converging evidence from lesion and neuroimaging studies that this region contributes to analyses of slow acoustic variations representing suprasegmental aspects of the speech signal (Ivry and Robertson, 1998; Johnsrude et al., 2000; Meyer et al., 2002; Poeppel et al., 2004; Zatorre, 2001). In line with the assumption that such analyses are crucial for identification of affective prosody, task-specific activations within the posterior middle temporal gyrus/superior temporal sulcus of the right hemisphere have been described in previous neuroimaging studies that contrasted evaluation of affective prosody with a control task in which the attention of the subject is directed to segmental aspects of the speech signal, such as semantics (Mitchell et al., 2003) or vocal identification (Wildgruber et al., 2005), while no task-specific activations within this region were found if the control task also requires suprasegmental analyses, such as evaluation of linguistic prosody (Wildgruber et al., 2004).

In addition to the right temporal cortex, bilateral activations within the middle/inferior frontal cortex were found in the present study during judgment of affective prosody. This finding runs counter with the idea that processing of emotions is an exclusive role of the right hemisphere. Lesion studies point to a disproportionately important role of the right hemisphere for perception and

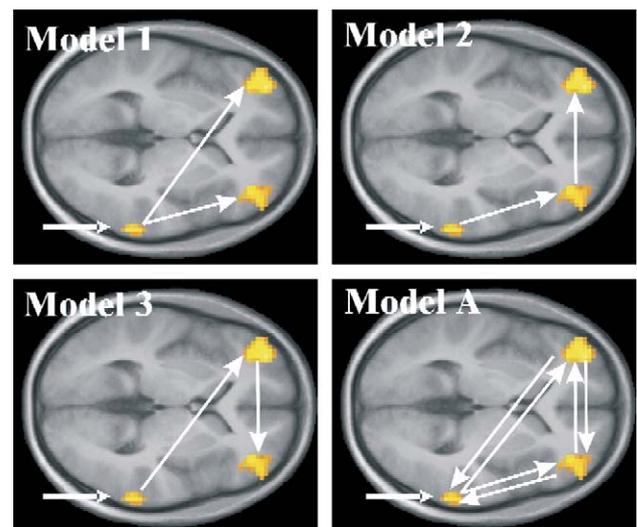


Fig. 4. Models on the intrinsic connectivity of regions involved in processing of affective prosody included a model with parallel information conductance from the temporal cortex to the two frontal regions (Model 1), two serial models with the temporal cortex as starting point (Models 2 and 3), and a model in which all regions were connected bidirectionally (Model A). In all these models, external inputs were specified to enter the network via the right temporal cortex.

Table 2

Model comparisons on intrinsic connectivity for brain regions involved in comprehension of emotional prosody on the basis of group Bayes factors as determined by Eq. (2) and binomial P values as determined by Eq. (3)

	Model 1	Model 2	Model 3	Model A
Model 1		$B_{21} = 1.43 \times 10^{-155}$ $P > 0.999$	$B_{31} = 1.50 \times 10^{-11}$ $P = 0.989$	$B_{A1} = 1.50 \times 10^{-205}$ $P > 0.999$
Model 2	$B_{12} = 6.99 \times 10^{154}$ $P < 0.001$		$B_{32} = 9.53 \times 10^{-145}$ $P = 0.729$	No evidence ^a $P = 0.924$
Model 3	$B_{13} = 6.66 \times 10^{10}$ $P = 0.011$	$B_{23} = 9.53 \times 10^{-147}$ $P = 0.271$		$B_{A3} = 1.61 \times 10^{-187}$ $P > 0.999$
Model A	$B_{1A} = 6.66 \times 10^{204}$ $P < 0.001$	No evidence ^a $P = 0.076$	$B_{3A} = 6.20 \times 10^{186}$ $P < 0.001$	

^a No evidence since Bayes factors as determined by AIC and BIC do not point to the same model.

recognition of affective prosody (Blonder et al., 1991; Bowers et al., 1987; Borod et al., 2002). However, it has been shown that patients with left hemispheric lesions sometimes also exhibit deficits in recognition of emotional speech melody (Adolphs et al., 2002; Hornak et al., 1996; Kucharska-Pietura et al., 2003; Pell, 1998; van Lancker and Sidtis, 1992). Recently, it has been demonstrated that circumscribed unilateral lesions of the inferior frontal cortex of either side can severely impair identification of emotional information in vocal expressions (Hornak et al., 2003) suggesting that both hemispheres, and specifically the frontal lobes, cooperate in decoding of affective prosody (for extensive review see Pell, 2002). In line with this suggestion, results from this study as well as previous functional imaging studies documented bilateral activations of the frontal cortex during evaluation of affective prosody (Imaizumi et al., 1997; Wildgruber et al., 2004). In some neuroimaging studies, activation was only described in the right inferior frontal cortex (George et al., 1996; Buchanan et al., 2000; Wildgruber et al., 2005). However, it should always be kept in mind that the absence of a significant activation does not enable to make an inference on the absence of an effect. In fact, in one of the studies published by our group (Wildgruber et al., 2005), activation within left inferior frontal cortex was not reported because it scarcely failed to reach the statistical threshold.

We used dynamic causal modeling to investigate the effective connectivity of the brain regions found to be involved in the processing of affective prosody as determined by a conventional fMRI analysis. Estimation of mean signal intensities yielded similar values for both frontal areas and the right middle temporal gyrus indicating that estimation of coupling parameters was not compromised by signal drop outs. Furthermore, all three brain regions were located within the same or adjacent slices ensuring that model estimation was not affected by differences in acquisition time. In agreement with our assumption, models in which the external input was specified to the right posterior temporal cortex were superior to models in which one of the frontal brain regions served as input region. This finding is in agreement with the view that comprehension of affective prosody requires prior evaluation of suprasegmental language features within the temporal cortex.

With respect to the intrinsic connectivity structure, various competing models for processing of affective speech melody were compared. In one type of models, a serial model structure was defined, in which left and right middle/inferior frontal cortices conduct sequential processing steps in decoding of emotional information. In the other type of model, a parallel connectivity pattern was specified assuming that frontal cortices of both hemispheres receive their information independently from the

right secondary auditory cortex. Comparison of the models based on their evidence as computed by a Bayesian approach and binomial group analysis revealed superiority of the latter model type over the first suggesting that frontal cortices of both hemispheres receive their information via parallel pathways. Furthermore, the parallel model was also superior to all models in which additional unidirectional or bidirectional connections between left and right frontal cortices were defined. The divergence of information conductance in the parallel model runs counter with the idea that evaluation of affective prosody occurs within one spatially defined brain area. However, as has been shown, integration of information in spatially distinct brain regions can occur via temporal coherence of neural activity (Bressler et al., 1993; Singer, 1993). A lack of temporal coherence could explain why unilateral lesions of the inferior frontal cortex of both left and right hemisphere impair recognition of affective prosody (Hornak et al., 2003).

Cortical networks subserving the perception and understanding of emotional word content

Regions showing a stronger BOLD response during evaluation of emotional word content as compared to rating of speech melody included the left temporal pole, left orbitofrontal cortex, and left superior frontal gyrus. To our knowledge, there is only one study in which task-specific hemodynamic responses during evaluation of the semantic attribute of emotional connotation were investigated (Crosson et al., 2002). In this study, BOLD responses during evaluation of emotional word content were compared to BOLD responses during pitch discrimination of simple tones. Given the difference in the control tasks between this study (pitch discrimination) and our study (rating of affective prosody), the finding of almost identical activation patterns is striking.

The left anterior temporal lobe is the region most consistently and seriously affected in patients with semantic dementia, a neurodegenerative disease characterized by progressive loss of expressive and receptive vocabulary (Mummery et al., 1999, 2000). Moreover, functional activation studies in healthy subjects have documented an involvement of the lateral cortex of the anterior temporal lobe in semantic associative processing (Vandenberghe et al., 1996; Price et al., 1996; Kellenbach et al., 2005). Therefore, activation within this region found in the present and in a previously published study (Crosson et al., 2002) on evaluation of emotional word content might correspond to mapping of speech features onto their lexical representations (Binder et al., 2004; Scott and Johnsrude, 2003).

While the temporal lobes are thought to be involved in the storage of semantic memories, a more executive role in selection of task-relevant information is attributed to the left inferior frontal cortex (Fiez, 1997). Thus, selection of emotional connotation as target information from competing semantic alternatives might constitute a possible explanation for the activation in the left orbitofrontal region (BA45/47) found in our study.

Enhanced BOLD responses within the left superior frontal gyrus (BA8/9/32) have been described during silent generation of emotional words of both negative and positive connotation as compared to neutral words (Crosson et al., 1999; Cato et al., 2004). Task-specific responses in this brain region during rating of emotional word content on a 9-point SAM scale in our study and previous results on classification of emotional word content in either positive or negative (Crosson et al., 2002) complement these findings and suggest that similar brain structures might be involved in input and output systems concerned with emotional word content. However, it is not likely that processing within the left medial superior frontal gyrus is restricted to emotional aspects of word meaning since activation in this region was also demonstrated during semantic interpretation of whether a noun is human-related or not (Scott et al., 2003) suggesting that this cortical region might be more generally concerned with choice between alternative semantic interpretations.

Note that acquisition of functional imaging data in axial plane in combination with a repetition time of 2.26 s in our study precludes valid inferences on the connectivity architecture of brain regions involved in comprehension of verbal emotional information. Axial slice orientation was chosen to minimize misspecifications in timing induced by sequential slice selection within the network concerned with processing of affective prosody. However, this resulted in a delay of roughly 2 s in data acquisition for brain regions specifically contributing to evaluation of emotional semantics (e.g. temporal pole and medial superior frontal gyrus) which is not acceptable for estimation of neural coupling parameters between such regions (Friston et al., 2003). In future studies on the intrinsic connectivity structure of brain areas involved in processing of affective word meaning, functional imaging data should be acquired in coronal or sagittal slice orientation to avoid delays in data acquisition between the implicated regions.

Limitations

By enabling inferences on coupling of neural states among brain areas, dynamic causal modeling extends traditional approaches in fMRI analysis which are restricted to investigation of regional activations. It also represents a more realistic approach on modeling brain function as compared to conventional approaches in which interactions between neural populations do not occur by definition (Friston et al., 2003). However, it is important to acknowledge the limitations of this technique in general and of the approach used in this study in particular. An important limitation of the models tested here arises from the definition of brain regions included in the models which relied on contrasting the hemodynamic response during rating of verbal and non-verbal emotional information. Neural areas which are equally involved in both of these tasks might have been precluded by this procedure. Therefore, the models tested might be incomplete with respect to the included brain regions. Furthermore, dynamic causal modeling is not an exploratory technique rendering the “best” model (Friston et al., 2003). This becomes immediately obvious when considering the degrees of

freedom available in specification of the model structure, rendering 2 to the power of $n * (n - 1)$ possible intrinsic connectivity patterns for models with n regions. Comparison of dynamic causal models by the use of Bayes factors can be used to test models corresponding to competing hypotheses about the intrinsic connectivity pattern of brain regions involved in a specific task (Penny et al., 2004). Such comparisons, however, only indicate a relative superiority of one model over another. To ensure that the superior model is not just the better alternative of two senseless models, we consider a model only to contain useful information if it explains the data and with a higher efficacy than a model in which all regions are connected bidirectionally with each other.

Conclusion

Conventional analysis of fMRI data yielded task-specific BOLD responses during rating of affective prosody in the right posterior temporal cortex and bilateral middle/inferior frontal cortices. Dynamic causal modeling was used to investigate the connectivity structure within this network. Bayes factors were employed to compare models with different intrinsic connectivity patterns and input regions. Models assuming external inputs in the right posterior temporal cortex were superior to models in which inputs were defined for one of the frontal regions indicating that comprehension of emotional speech melody requires prior processing of acoustic information within the right temporal cortex. Superiority of the model assuming that the two frontal regions receive their information independent from each other as compared to models in which the two frontal cortices conduct serial processing steps suggests that frontal cortices receive their information via parallel pathways.

Acknowledgments

This study was supported by the Deutsche Forschungsgemeinschaft (DFG grant WI 2101/1-1) and by the Junior Science Program of the Heidelberger Academy of Sciences and Humanities.

References

- Adolphs, R., Damasio, H., Tranel, D., 2002. Neural systems for recognition of emotional prosody: a 3-D lesion study. *Emotion* 2, 23–51.
- Banse, R., Scherer, K.R., 1996. Acoustic profiles in vocal emotion expression. *J. Pers. Soc. Psychol.* 70, 614–636.
- Blonder, L.X., Bowers, D., Heilmann, K., 1991. The role of the right hemisphere in emotional communication. *Brain* 114, 1115–1127.
- Binder, J.R., Liebenthal, E., Possing, E.T., Medler, D.A., Ward, B.D., 2004. Neural correlates of sensory and decision processes in auditory object identification. *Nat. Neurosci.* 7, 295–301.
- Borod, J.C., Bloom, R.L., Brickman, A.M., Nakhutina, L., Curko, E.A., 2002. Emotional processing deficits in individuals with unilateral brain damage. *App. Neuropsychol.* 9, 23–36.
- Bowers, D., Coslett, H.B., Bauer, R.M., Speedie, L.J., Heilmann, K.H., 1987. Comprehension of emotional prosody following unilateral hemispheric lesions: processing defect versus distraction defect. *Neuropsychologia* 25, 317–328.
- Bradley, M.M., Lang, P.J., 1994. Measuring emotion: the self-assessment manikin and the semantic differential. *J. Behav. Ther. Exp. Psychiatry* 25, 49–59.
- Bressler, S., Coppola, R., Nakamura, R., 1993. Episodic multiregional

- cortical coherence at multiple frequencies during visual task performance. *Nature* 366, 153–156.
- Buchanan, T.W., Lutz, K., Mirzazade, S., Specht, K., Shah, N.J., Zilles, K., Jäncke, L., 2000. Recognition of emotional prosody and verbal components of spoken language: an fMRI study. *Cogn. Brain Res.* 9, 227–238.
- Cato, M.A., Crosson, B., Gokcay, D., Soltysik, D., Wierenga, C., Gopinath, K., Himes, N., Belanger, H., Bauer, R.M., Fischler, I.S., Gonzalez-Rothi, L., Briggs, R.W., 2004. Processing words with emotional connotation: an FMRI study of time course and laterality in rostral frontal and retrosplenial cortices. *J. Cogn. Neurosci.* 16, 167–177.
- Collins, D.L., Neelin, P., Peters, T.M., Evans, A.C., 1994. Automatic 3D intersubject registration of MR volumetric data in standardized Talairach space. *J. Comput. Assist. Tomogr.* 18, 192–205.
- Crosson, B., Radonovich, K., Sadek, J.R., Gökçay, D., Bauer, R.M., Fischler, I.S., Cato, M.A., Maron, L., Auerbach, E.J., Browd, S.R., Briggs, R.W., 1999. Left hemisphere processing of emotional connotation during word generation. *NeuroReport* 10, 2449–2455.
- Crosson, B., Cato, M.A., Sadek, J.R., Gökçay, D., Bauer, R.M., Fischler, I.S., Maron, L., Gopinath, K., Auerbach, E.J., Browd, S.R., Briggs, R.W., 2002. Semantic monitoring of words with emotional connotation during fMRI: contribution of anterior left frontal cortex. *J. Int. Neuropsychol. Soc.* 8, 607–622.
- Fiez, J.A., 1997. Phonology, semantics, and the role of the left inferior prefrontal cortex. *Hum. Brain Mapp.* 5, 79–83.
- Friston, K.J., Glaser, D.E., Henson, R.N.A., Kiebel, S., Phillips, C., Ashburner, J., 2002. Classical and bayesian inference in neuroimaging: applications. *NeuroImage* 16, 484–512.
- Friston, K.J., Harrison, L., Penny, W., 2003. Dynamic causal modelling. *NeuroImage* 19, 1273–1302.
- George, M.S., Parekh, P.I., Rosinsky, N., Ketter, T.A., Kimbrell, T.A., Heilmann, K.M., Herscovitch, P., Post, R.M., 1996. *Arch. Neurol.* 53, 665–670.
- Herbert, C., Kissler, J., Junghöfer, M., Peyk, P., Rockstroh, B., submitted for publication. Startle modulation during affective word processing. *Psychophysiology*.
- Hornak, J., Rolls, E.T., Wade, D., 1996. Face and voice expression identification in patients with emotional and behavioural changes following ventral frontal lobe damage. *Neuropsychologia* 34, 247–261.
- Hornak, J., Bramham, J., Rolls, E.T., Morris, R.G., O'Doherty, J., Bullock, P.R., Polkey, C.E., 2003. Changes in emotion after circumscribed surgical lesions of the orbitofrontal and cingulate cortices. *Brain* 126, 1691–1712.
- Imaizumi, S., Mori, K., Kiritani, S., Kawashima, R., Sugiura, M., Fukuda, H., Itoh, K., Kato, T., Nakamura, A., Hatano, K., Kojima, S., Nakamura, K., 1997. Vocal identification of speaker and emotion activates different brain regions. *NeuroReport* 8, 2809–2812.
- Ivry, R.B., Robertson, L.C., 1998. *The Two Sides of Perception*. MIT Press, Cambridge, MA.
- Jäncke, L., Wüstenberg, T., Scheich, H., Heinze, H.J., 2002. Phonetic perception and the temporal cortex. *NeuroImage* 15, 733–746.
- Johnsrude, I.S., Penhune, V.B., Zatorre, R.J., 2000. Functional specificity in the right human auditory cortex for perceiving pitch direction. *Brain* 123, 155–163.
- Kellenbach, M.L., Hovius, M., Patterson, K., 2005. A PET study of visual and semantic knowledge about objects, 2005. *Cortex* 41, 121–132.
- Kucharska-Pietura, K., Phillips, M.L., Gernand, W., David, A.S., 2003. Perception of emotions from faces and voices following unilateral brain damage. *Neuropsychologia* 41, 1082–1090.
- Meyer, M., Alter, K., Friederici, A.D., Lohmann, G., von Cramon, D.Y., 2002. FMRI reveals brain regions mediating slow prosodic modulations in spoken sentences. *Hum. Brain Mapp.* 17, 73–88.
- Mitchell, R.L., Elliott, R., Barry, M., Cruttenden, A., Woodruff, P.W., 2003. The neural response to emotional prosody, as revealed by functional magnetic resonance imaging. *Neuropsychologia* 41, 1410–1421.
- Mummary, C.J., Patterson, K., Wise, R.J.S., Vandenberghe, R., Price, C.J., Hodges, J.R., 1999. Disrupted temporal lobe connections in semantic dementia. *Brain* 122, 61–73.
- Mummary, C.J., Patterson, K., Price, C.J., Ashburner, J., Frackowiak, R.S.J., Hodges, J.R., 2000. *Ann. Neurol.* 47, 36–45.
- Oldfield, R.C., 1971. Assessment and analysis of handedness: the Edinburgh inventory. *Neuropsychologia* 9, 97–113.
- Pell, M., 1998. Recognition of prosody following unilateral brain lesion: influence of functional and structural attributes of prosodic contours. *Neuropsychologia* 36, 701–715.
- Pell, M.D., 2002. Surveying emotional prosody in the brain. In: Bel, B., Marlien, I. (Eds.), *Proceedings of Speech Prosody, 2002 Conference*, 11–13 April, 2002. Aix-en Provence, Laboratoire Parole et Langage, pp. 77–82.
- Penny, W., Stephan, K.E., Mechelli, A., Friston, K.J., 2004. Comparing dynamic causal models. *NeuroImage* 22, 1157–1172.
- Pihan, H., Altenmüller, E., Hertrich, I., Ackermann, H., 2000. Cortical activation patterns of affective speech processing depend on concurrent demands on the subvocal rehearsal system. A DC-potential study. *Brain* 123, 2338–2349.
- Poeppel, D., Guillemin, A., Thompson, J., Fritz, J., Bavelier, D., Braun, A., 2004. Auditory lexical decision, categorial perception, and FM direction discrimination differentially engage left and right auditory cortex. *Neuropsychologia* 42, 183–200.
- Price, C.J., Moore, C.J., Humphreys, G.W., Frackowiak, R.S., Friston, K.J., 1996. The neural regions sustaining object recognition and naming. *Proc. Biol. Sci.* 263, 1501–1507.
- Ross, E.D., Thompson, R.D., Yenkosky, J., 1997. Lateralization of affective prosody in brain and the callosal integration of hemispheric language functions. *Brain Lang.* 56, 27–54.
- Scott, S.K., Johnsrude, I.S., 2003. The neuroanatomical and functional organization of speech perception. *Trends Neurosci.* 26, 100–107.
- Scott, S.K., Leff, A.P., Wise, R.J.S., 2003. Going beyond the information given: a neural system supporting semantic interpretation. *NeuroImage* 19, 870–876.
- Singer, W., 1993. Neuronal representations and temporal codes. In: Poggio, T.A., Glaser, D.A. (Eds.), *Exploring Brain Functions: Models in Neuroscience*. John Wiley & Sons Ltd., Chichester, pp. 179–194.
- Tzourio-Mazoyer, N., Landeau, B., Papathanassiou, D., Crivello, F., Etard, O., Delcroix, N., Mazoyer, B., Joliot, M., 2002. Automated anatomical labeling of activations in SPM using a macroscopic anatomical parcellation of the MNI MRI single-subject brain. *NeuroImage* 15, 273–289.
- van Lancker, D., Sidtis, J.J., 1992. The identification of affective-prosodic stimuli by left- and right-hemisphere-damaged subjects: all errors are not created equal. *J. Speech Hear. Res.* 35, 963–970.
- Vandenberghe, R., Price, C., Wise, R., Josephs, O., Frackowiak, R.S.J., 1996. Functional anatomy of a common semantic system for words and pictures. *Nature* 383, 254–256.
- Wildgruber, D., Pihan, H., Ackermann, H., Erb, M., Grodd, W., 2002. Dynamic brain activation during processing of emotional intonation: influence of acoustic parameters, emotional valence, and sex. *NeuroImage* 15, 856–869.
- Wildgruber, D., Hertrich, I., Riecker, A., Erb, M., Anders, S., Grodd, W., Ackermann, H., 2004. Distinct frontal regions subserve evaluation of linguistic and emotional aspects of speech intonation. *Cereb. Cortex* 14, 1384–1389.
- Wildgruber, D., Riecker, A., Hertrich, I., Erb, M., Grodd, W., Ethofer, T., Ackermann, H., 2005. Identification of emotional intonation evaluated by fMRI. *NeuroImage* 24, 1233–1241.
- Zatorre, R.J., 2001. Neural specializations for tonal processing. *Ann. N. Y. Acad. Sci.* 930, 193–210.